

chain nodes :

5 6 7 8 9 14 15 16 17 18

ring nodes :

1 2 3 4

chain bonds :

1-5 3-6 6-7 7-8 7-14 8-9 9-18 14-15 14-16 17-18

ring bonds :

1-2 1-4 2-3 3-4

exact/norm bonds :

1-5 3-6 6-7 7-8 8-9 9-18 14-15 14-16 17-18

exact bonds :

1-2 1-4 2-3 3-4 7-14

isolated ring systems :

containing 1 :

G1:O,S

G2:O,S,N

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:CLASS 6:CLASS 7:CLASS 8:CLASS
9:Atom 14:CLASS 15:CLASS 16:CLASS 17:Atom 18:CLASS

10/081,072

STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

=> s l10 sss full

FULL SEARCH INITIATED 12:03:33 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 73051 TO ITERATE

100.0% PROCESSED 73051 ITERATIONS

SEARCH TIME: 00.00.02

0 ANSWERS

L11 0 SEA SSS FUL L10

=>

Uploading C:\Program Files\Stnexp\Queries\081072.str

L12 STRUCTURE UPLOADED

=> d l12

L12 HAS NO ANSWERS

L12 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

=> s l12 sss full

FULL SEARCH INITIATED 12:06:03 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 1009 TO ITERATE

100.0% PROCESSED 1009 ITERATIONS

SEARCH TIME: 00.00.01

756 ANSWERS

L13 756 SEA SSS FUL L12

=> file caplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

625.04

965.51

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

CA SUBSCRIBER PRICE

0.00

-4.16

FILE 'CAPLUS' ENTERED AT 12:06:09 ON 25 JUN 2004

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10/081,072

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FILE COVERS 1907 - 25 Jun 2004 VOL 141 ISS 1
FILE LAST UPDATED: 24 Jun 2004 (20040624/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l13

L14 14 L13

=> d l14 1-14 ibib abs hitstr

L14 ANSWER 1 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:892751 CAPLUS

DOCUMENT NUMBER: 139:381384

TITLE: Preparation of 2,6-quinolinyl and 2,6-naphthyl(acylamino)propionic acids as VLA-4 inhibitors

INVENTOR(S): Lassoie, Marie-Agnes; Knerr, Laurent; Demaude, Thierry; De Laveleye, Francoise; Kogej, Thierry; Routier, Sylvain; Guillaumet, Gerald

PATENT ASSIGNEE(S): UCB, S.A., Belg.

SOURCE: PCT Int. Appl., 122 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

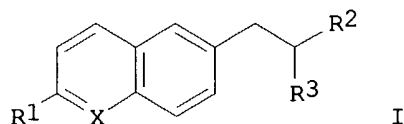
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003093237	A1	20031113	WO 2003-EP3909	20030415
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.: EP 2002-9746 A 20020430

OTHER SOURCE(S): MARPAT 139:381384

GI



AB Title compds. I [X = N, CH; R1 = R1 = cycloalkyl, aryl, hewterocyclic,

heterocyclalkyl, substituted OH, norbornen-5-yl; R2 = (un)substituted NH2, OH, CONH2; R3 = tetrazolyl, CN, CH2OH, (un)substituted CO2H] were prepared for use in treating VLA-4 dependent inflammatory diseases such as asthma, allergic rhinitis, sinusitis, conjunctivitis, food allergy, psoriasis, urticaria, pruritus, eczema, rheumatoid arthritis, inflammatory bowel disease, multiple sclerosis and atherosclerosis (no data). Thus, 4-nitrophenylalanine was esterified, N-protected, reduced to the amine, cyclized with 2,6-Cl2C6H3CHO and CH2:CHSPh, followed by elimination of PhSH to give I [X = N, R1 = 2,6-Cl2C6H3, R2 = NHBoc, R3 = CO2Me]. This compound was deprotected and acylated with 2,6-Cl2C6H3COCl, followed by ester hydrolysis to give I [X = N, R1 = 2,6-Cl2C6H3, R2 = 2,6-Cl2C6H3CONH, R3 = CO2H].

IT **623145-12-0P 623145-19-7P**

RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use);

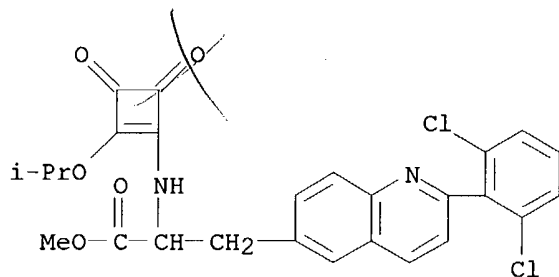
BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent);

USES (Uses)

(preparation of 2,6-quinolinyl and 2,6-naphthyl(acylamino)propionic acids as VLA-4 inhibitors)

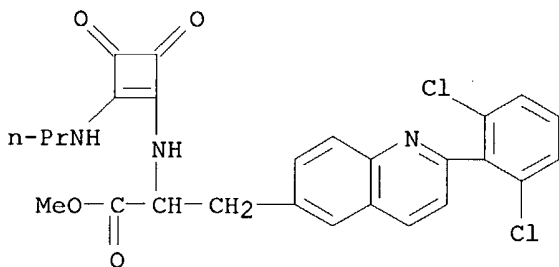
RN 623145-12-0 CAPLUS

CN 6-Quinolinepropanoic acid, 2-(2,6-dichlorophenyl)- α -[[2-(1-methylethoxy)-3,4-dioxo-1-cyclobuten-1-yl]amino]-, methyl ester (9CI) (CA INDEX NAME)



RN 623145-19-7 CAPLUS

CN 6-Quinolinepropanoic acid, 2-(2,6-dichlorophenyl)- α -[[3,4-dioxo-2-(propylamino)-1-cyclobuten-1-yl]amino]-, methyl ester (9CI) (CA INDEX NAME)



IT **623146-06-5P**

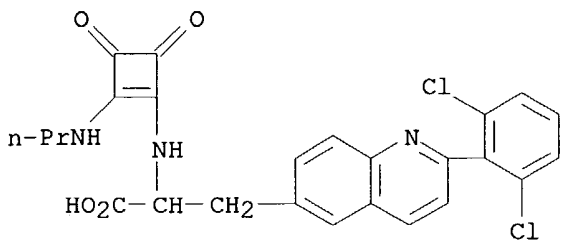
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 2,6-quinolinyl and 2,6-naphthyl(acylamino)propionic acids as VLA-4 inhibitors)

RN 623146-06-5 CAPLUS

CN 6-Quinolinepropanoic acid, 2-(2,6-dichlorophenyl)- α -[[3,4-dioxo-2-

(propylamino)-1-cyclobuten-1-yl]amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:435940 CAPLUS

DOCUMENT NUMBER: 139:149503

TITLE: Efficient Synthesis of 3-Aminocyclobut-2-en-1-ones:
Squaramide Surrogates as Potent VLA-4 Antagonists
AUTHOR(S): Brand, Stephen; De Candole, Benjamin C.; Brown, Julien A.

CORPORATE SOURCE: Medicinal Chemistry, Celltech Group plc, Slough, SL1 4EN, UK

SOURCE: Organic Letters (2003), 5(13), 2343-2346
CODEN: ORLEF7; ISSN: 1523-7060

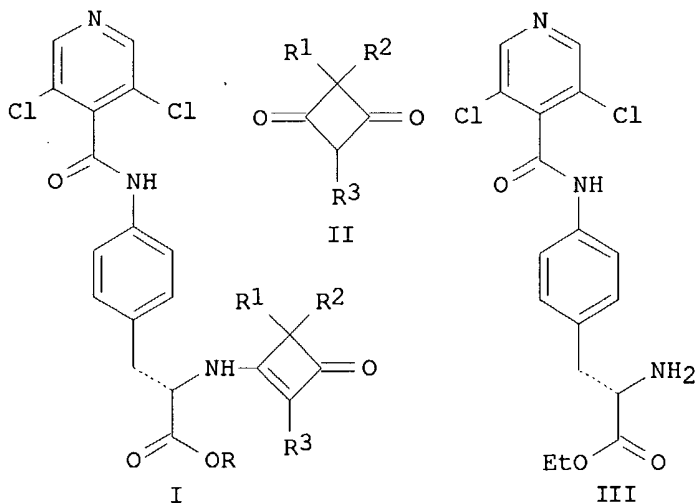
PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 139:149503

GI



AB A novel series of uniquely functionalized 3-aminocyclobut-2-en-1-ones I [R = Et, R1 = Me, R2 = Me, Ph, CH2Ph, R3 = H; R = Et, R1R2 = (CH2)n, n = 4-6, R3 = H; R = Et, R1R2 = (CH2)2O(CH2)2, R3 = H; R = Et, R1 = R2 = Me, R3 = CH2Ph, Me, n-Pr, etc.; etc.] has been prepared by facile condensation of a

10/081,072

variety of cyclobuta-1,3-diones II with a phenylalanine-derived primary amine III. These systems subsequently lend themselves to substitution at C-2 by reaction with a variety of electrophilic reagents including N-halosuccinimides, sulfonyl chlorides, and Eschenmoser's salt, to get new analogs I [R = Et, R1R2 = (CH2)5, R3 = Br, SPh, SePh, etc.]. Compds. I (R = H) from this novel series are potent antagonists of VLA-4.

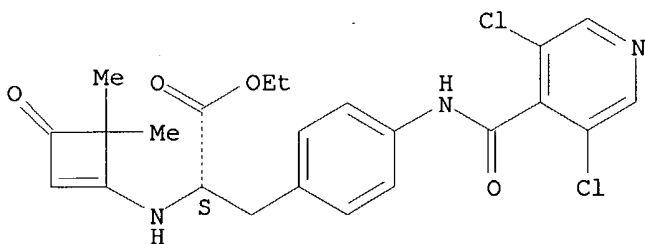
IT **455262-11-0P 455262-24-5P 455262-34-7P**
455263-48-6P 455263-52-2P 455263-71-5P
455263-73-7P 455263-75-9P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of phenylalanine-derived 3-aminocyclobut-2-en-1-ones as VLA-4 antagonists)

RN 455262-11-0 CAPLUS

CN L-Phenylalanine, 4-[[[(3,5-dichloro-4-pyridinyl)carbonyl]amino]-N-(4,4-dimethyl-3-oxo-1-cyclobuten-1-yl)-, ethyl ester (9CI) (CA INDEX NAME)

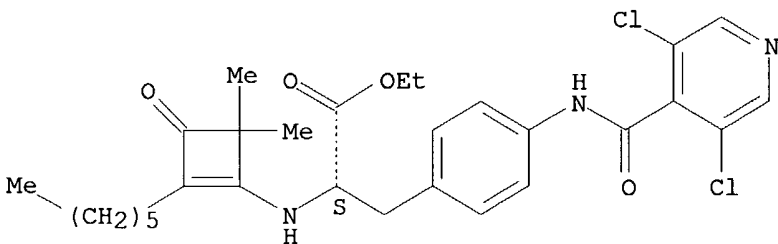
Absolute stereochemistry.



RN 455262-24-5 CAPLUS

CN L-Phenylalanine, 4-[[[(3,5-dichloro-4-pyridinyl)carbonyl]amino]-N-(2-hexyl-4,4-dimethyl-3-oxo-1-cyclobuten-1-yl)-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

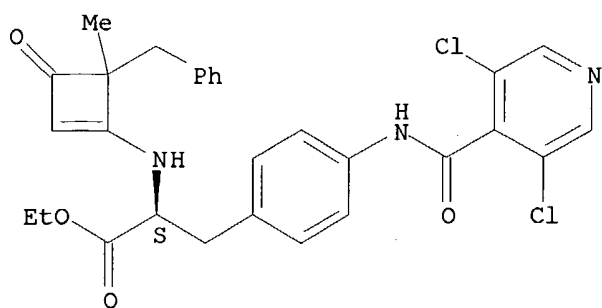


RN 455262-34-7 CAPLUS

CN L-Phenylalanine, 4-[[[(3,5-dichloro-4-pyridinyl)carbonyl]amino]-N-[4-methyl-3-oxo-4-(phenylmethyl)-1-cyclobuten-1-yl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

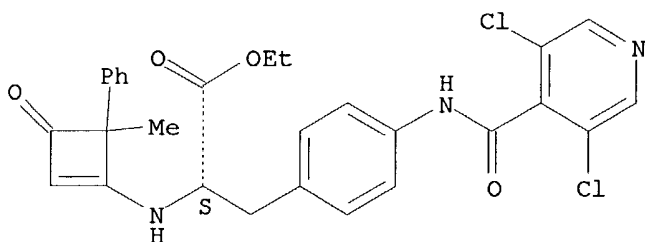
10/081,072



RN 455263-48-6 CAPLUS

CN L-Phenylalanine, 4-[[(3,5-dichloro-4-pyridinyl)carbonyl]amino]-N-(4-methyl-3-oxo-4-phenyl-1-cyclobuten-1-yl)-, ethyl ester (9CI) (CA INDEX NAME)

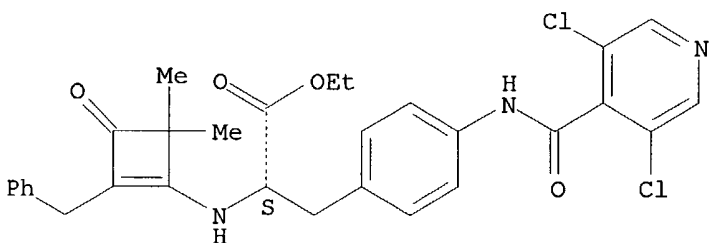
Absolute stereochemistry.



RN 455263-52-2 CAPLUS

CN L-Phenylalanine, 4-[[(3,5-dichloro-4-pyridinyl)carbonyl]amino]-N-[4,4-dimethyl-3-oxo-2-(phenylmethyl)-1-cyclobuten-1-yl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

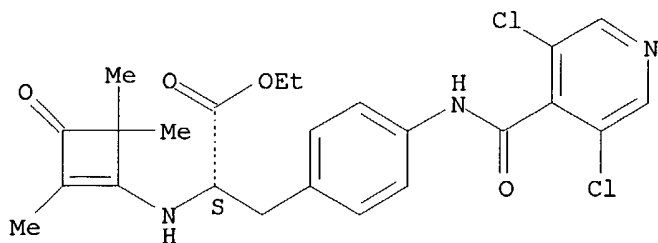


RN 455263-71-5 CAPLUS

CN L-Phenylalanine, 4-[[(3,5-dichloro-4-pyridinyl)carbonyl]amino]-N-(2,4,4-trimethyl-3-oxo-1-cyclobuten-1-yl)-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

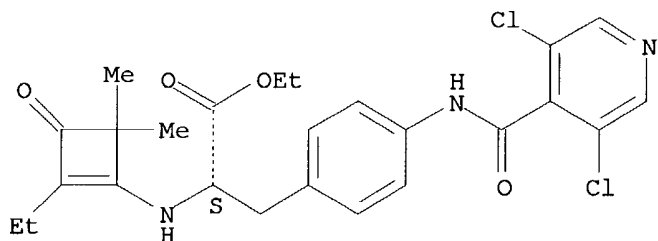
10/081,072



RN 455263-73-7 CAPLUS

CN L-Phenylalanine, 4-[[[(3,5-dichloro-4-pyridinyl)carbonyl]amino]-N-(2-ethyl-4,4-dimethyl-3-oxo-1-cyclobuten-1-yl)-, ethyl ester (9CI) (CA INDEX NAME)

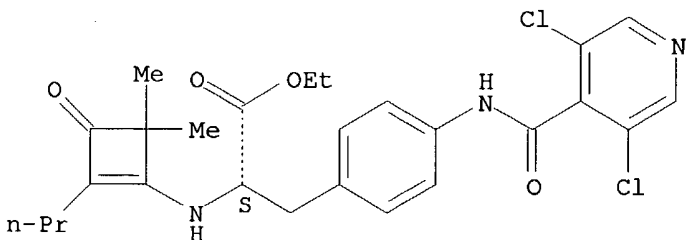
Absolute stereochemistry.



RN 455263-75-9 CAPLUS

CN L-Phenylalanine, 4-[[[(3,5-dichloro-4-pyridinyl)carbonyl]amino]-N-(4,4-dimethyl-3-oxo-2-propyl-1-cyclobuten-1-yl)-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 3 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:117787 CAPLUS

DOCUMENT NUMBER: 138:137592

TITLE: Preparation of bicyclic heteroaromatic alanines as α 4-integrin inhibitors

INVENTOR(S): Aujla, Pavandeep; Norman, Timothy John; Porter, John Robert; Bailey, Stuart; Brand, Stephen

PATENT ASSIGNEE(S): Celltech R & D Limited, UK

SOURCE: PCT Int. Appl., 97 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

10/081,072

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

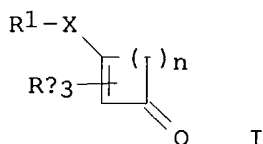
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003011815	A1	20030213	WO 2002-GB3400	20020725
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.: GB 2001-18241 A 20010726
GB 2001-26653 A 20011106

OTHER SOURCE(S): MARPAT 138:137592

GI



AB Compds. I [n = 1-4; X is O, S, NH, or alkylimino; R1 is a group Ar1-L2-Ar2-Alk-, in which Ar1 is an optionally-substituted (hetero)aromatic group, L2 is a covalent bond or a linker atom or group, Ar2 is an optionally substituted bicyclic heteroarylene group, and Alk is a chain CH2CHR, CH=CR, or CH(CH2R) (R is CO2H or a derivative or biostere); Rx are independently groups L1-Alk10-1-R31-3, in which L1 is a covalent bond or a linker atom or group, Alk1 is an optionally substituted (hetero)aliphatic chain, R3 is H, halo, OH, (cyclo)alkoxy, SH, (cyclo)alkylthio, CN, or an optionally substituted, (hetero)cycloaliph., (hetero)polycycloaliph., or (hetero)aromatic group; or two Rx are joined together to form an optionally-substituted spiro-linked (hetero)cycloaliph. group] were prepared as selective inhibitors of $\alpha 4$ integrins such as $\alpha 4\beta 1$ and are of use in modulating cell adhesion for the prophylaxis or treatment of inflammatory diseases or disorders, such as rheumatoid arthritis, in which the extravasulation of leukocytes plays a role. Thus, Me 3-[1-(3,5-dichloroisonicotinoyl)-2,3-dihydro-1H-indol-5-yl]-2-[(3-oxospiro[3.5]non-1-en-1-yl)amino]propanoate was prepared by condensing Me 2-amino-3-[1-(3,5-dichloroisonicotinoyl)-2,3-dihydro-1H-indol-5-yl]propanoate (preparation given) with spiro[3.5]nonane-1,3-dione. Compds. of the examples generally have IC50 values in the $\alpha 4\beta 1$ and $\alpha 4\beta 7$ assays of ≤ 1 and ≤ 5 μM , resp. IC50 values for α integrins of other subgroups were 50 μM , thus demonstrating the potency and selectivity of compds. of the invention against $\alpha 4$ integrins.

IT **494227-85-9P 494227-86-0P**

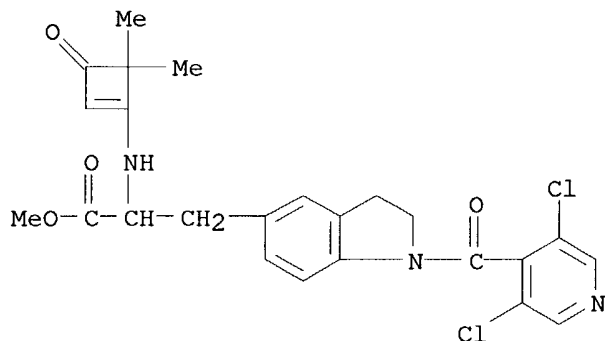
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

10/081,072

(preparation of bicyclic heteroarom. alanines as α 4-integrin inhibitors)

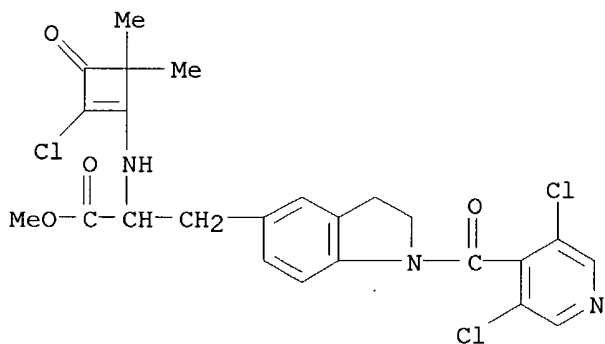
RN 494227-85-9 CAPLUS

CN 1H-Indole-5-propanoic acid, 1-[(3,5-dichloro-4-pyridinyl)carbonyl]- α -[(4,4-dimethyl-3-oxo-1-cyclobuten-1-yl)amino]-2,3-dihydro-, methyl ester (9CI) (CA INDEX NAME)



RN 494227-86-0 CAPLUS

CN 1H-Indole-5-propanoic acid, α -[(2-chloro-4,4-dimethyl-3-oxo-1-cyclobuten-1-yl)amino]-1-[(3,5-dichloro-4-pyridinyl)carbonyl]-2,3-dihydro-, methyl ester (9CI) (CA INDEX NAME)



IT 494227-87-1P 494227-88-2P

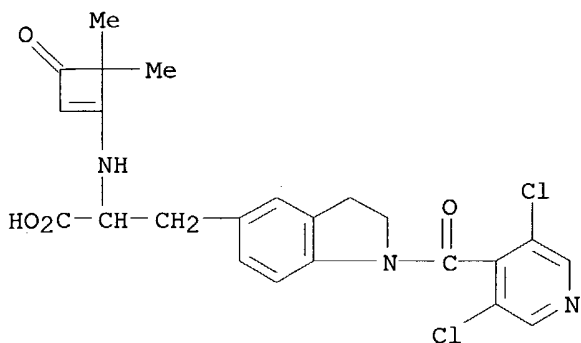
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of bicyclic heteroarom. alanines as α 4-integrin inhibitors)

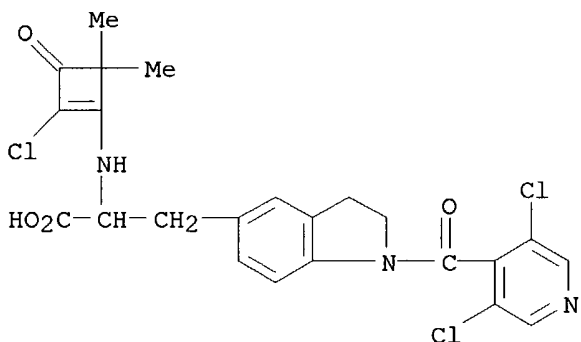
RN 494227-87-1 CAPLUS

CN 1H-Indole-5-propanoic acid, 1-[(3,5-dichloro-4-pyridinyl)carbonyl]- α -[(4,4-dimethyl-3-oxo-1-cyclobuten-1-yl)amino]-2,3-dihydro- (9CI) (CA INDEX NAME)

10/081,072



RN 494227-88-2 CAPLUS
CN 1H-Indole-5-propanoic acid, α -[(2-chloro-4,4-dimethyl-3-oxo-1-cyclobuten-1-yl)amino]-1-[(3,5-dichloro-4-pyridinyl)carbonyl]-2,3-dihydro-
(9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 4 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:675997 CAPLUS

DOCUMENT NUMBER: 137:217241

TITLE: Preparation of phenylalanine enamide derivatives possessing a cyclobutene group for use as integrin inhibitors

INVENTOR(S): Bailey, Stuart; Brown, Julien Alistair; Brand, Stephen; Johnson, James Andrew; Porter, John Robert; Head, John Clifford

PATENT ASSIGNEE(S): Celltech R & D Limited, UK

SOURCE: PCT Int. Appl., 201 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

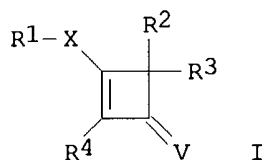
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002068393	A1	20020906	WO 2002-GB206	20020118
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,				

LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
 PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
 UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
 CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
 GB 2387845 A1 20031029 GB 2003-18429 20020118
 EP 1370531 A1 20031217 EP 2002-715515 20020118
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
 BR 2002007166 A 20040210 BR 2002-7166 20020118
 US 2002169336 A1 20021114 US 2002-81072 20020222
 NO 2003003710 A 20031022 NO 2003-3710 20030820
 PRIORITY APPLN. INFO.: GB 2001-4418 A 20010222
 GB 2001-14000 A 20010608
 GB 2001-27562 A 20011116
 WO 2002-GB206 W 20020118
 OTHER SOURCE(S): MARPAT 137:217241
 GI



AB Phenylalanine enamide derivs. I [R1 is a group Ar1-L2-Ar2-Alk- in which Ar1 is an optionally substituted (hetero)aromatic group, L2 is a covalent bond or a linker atom or group, Ar2 is an optionally substituted (hetero)arylene group, and Alk is CH2CHCO2H, CH:CCO2H, or CHCH2CO2H or a derivative or biostere; X = O, S, NH or alkylimino; V = O or S; R2, R3, R4 = L1-(Alk1)n(R5)v, in which L1 is a covalent bond or a linker atom or group, Alk1 is an optionally substituted (hetero)aliphatic chain, R5 = H, halo, OH, SH, CN, (un)substituted (cyclo)alkoxy, (cyclo)alkylthio, (hetero)(poly)cycloaliph. or (hetero)aromatic group; n = 0 or 1, and v = 1-3] were prepared. Compds. I inhibit the binding of integrins to their ligands and are of use in the prophylaxis and treatment of immuno or inflammatory disorders or disorders involving the inappropriate growth or migration of cells. Thus, (2S)-2-[(3-oxospiro[3.5]non-1-en-1-yl)amino]-3-[4-[(3,5-dichloroisonicotinoyl)amino]phenyl]propanoic acid (claimed compound) was prepared by reaction of Et (2S)-2-amino-3-[4-[(3,5-dichloroisonicotinoyl)amino]phenyl]propanoate (preparation given) with 1-keto-3-hydroxyspiro[3.5]non-2-ene, followed by hydrolysis.

IT 455262-06-3P 455262-09-6P 455262-11-0P
 455262-13-2P 455262-15-4P 455262-17-6P
 455262-20-1P 455262-22-3P 455262-24-5P
 455262-26-7P 455262-30-3P 455262-32-5P
 455262-34-7P 455262-43-8P 455262-60-9P
 455262-67-6P 455262-75-6P 455262-76-7P
 455263-04-4P 455263-09-9P 455263-42-0P
 455263-46-4P 455263-48-6P 455263-52-2P
 455263-71-5P 455263-73-7P 455263-75-9P
 455263-91-9P 455263-96-4P 455264-08-1P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

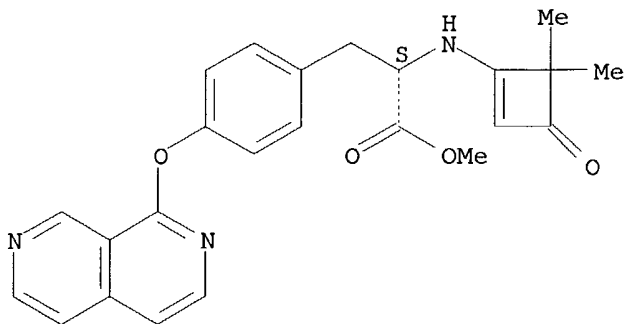
10/081,072

(preparation of phenylalanine enamide derivs. possessing a cyclobutene group
for use as integrin inhibitors)

RN 455262-06-3 CAPLUS

CN L-Tyrosine, N-(4,4-dimethyl-3-oxo-1-cyclobuten-1-yl)-O-2,7-naphthyridin-1-yl-, methyl ester (9CI) (CA INDEX NAME)

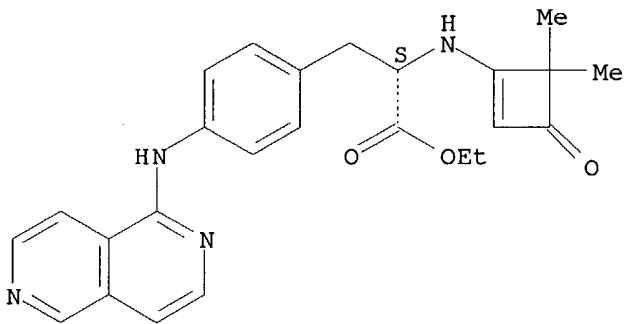
Absolute stereochemistry.



RN 455262-09-6 CAPLUS

CN L-Phenylalanine, N-(4,4-dimethyl-3-oxo-1-cyclobuten-1-yl)-4-(2,6-naphthyridin-1-ylamino)-, ethyl ester (9CI) (CA INDEX NAME)

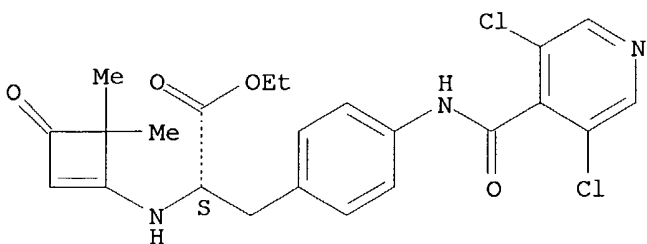
Absolute stereochemistry.



RN 455262-11-0 CAPLUS

CN L-Phenylalanine, 4-[[[(3,5-dichloro-4-pyridinyl)carbonyl]amino]-N-(4,4-dimethyl-3-oxo-1-cyclobuten-1-yl)-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

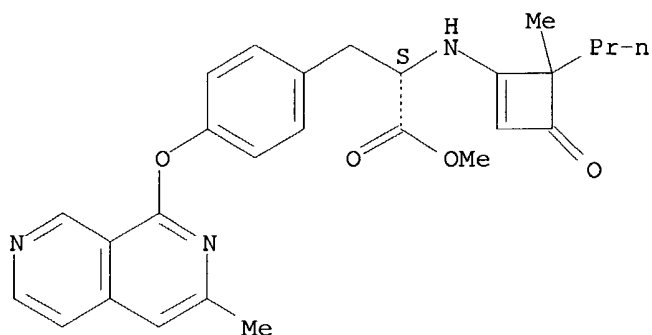


RN 455262-13-2 CAPLUS

CN L-Tyrosine, O-(3-methyl-2,7-naphthyridin-1-yl)-N-(4-methyl-3-oxo-4-propyl-1-cyclobuten-1-yl)-, methyl ester (9CI) (CA INDEX NAME)

10/081,072

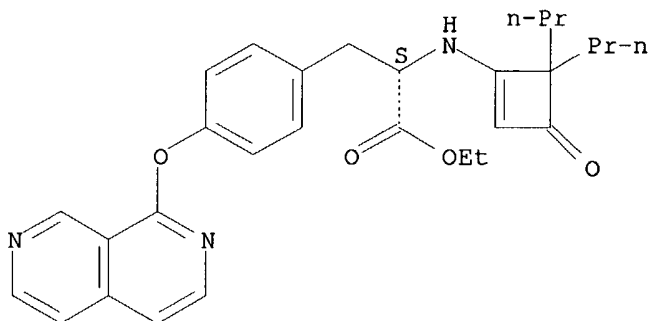
Absolute stereochemistry.



RN 455262-15-4 CAPLUS

CN L-Tyrosine, O-2,7-naphthyridin-1-yl-N-(3-oxo-4,4-dipropyl-1-cyclobuten-1-yl)-, ethyl ester (9CI) (CA INDEX NAME)

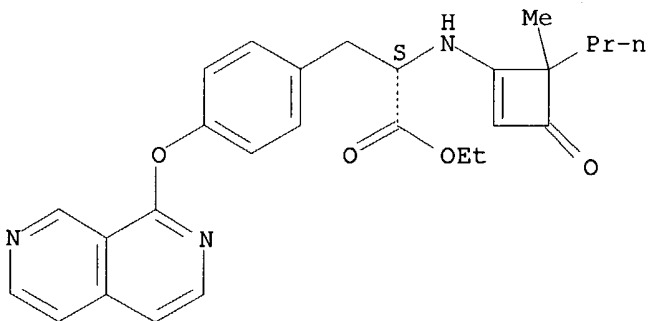
Absolute stereochemistry.



RN 455262-17-6 CAPLUS

CN L-Tyrosine, N-(4-methyl-3-oxo-4-propyl-1-cyclobuten-1-yl)-O-2,7-naphthyridin-1-yl-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

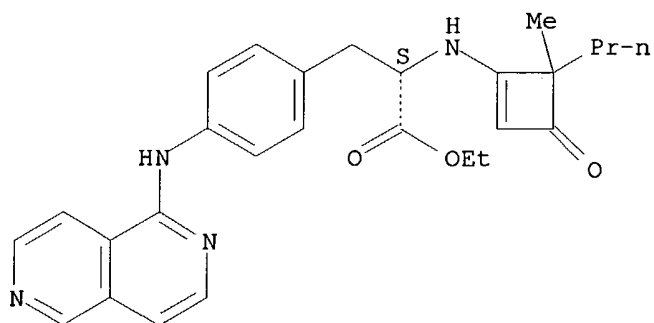


RN 455262-20-1 CAPLUS

CN L-Phenylalanine, N-(4-methyl-3-oxo-4-propyl-1-cyclobuten-1-yl)-4-(2,6-naphthyridin-1-ylamino)-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

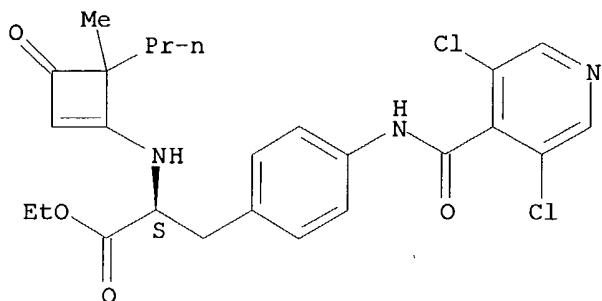
10/081,072



RN 455262-22-3 CAPLUS

CN L-Phenylalanine, 4-[[[(3,5-dichloro-4-pyridinyl)carbonyl]amino]-N-(4-methyl-3-oxo-4-propyl-1-cyclobuten-1-yl)-, ethyl ester (9CI) (CA INDEX NAME)

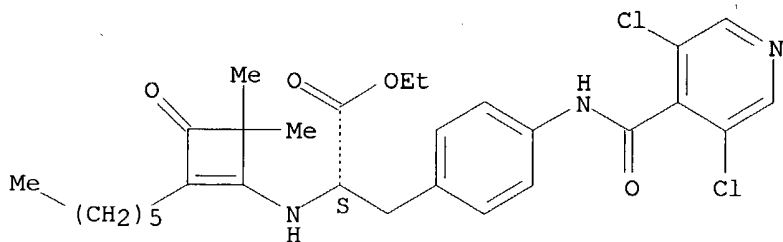
Absolute stereochemistry.



RN 455262-24-5 CAPLUS

CN L-Phenylalanine, 4-[[[(3,5-dichloro-4-pyridinyl)carbonyl]amino]-N-(2-hexyl-4,4-dimethyl-3-oxo-1-cyclobuten-1-yl)-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

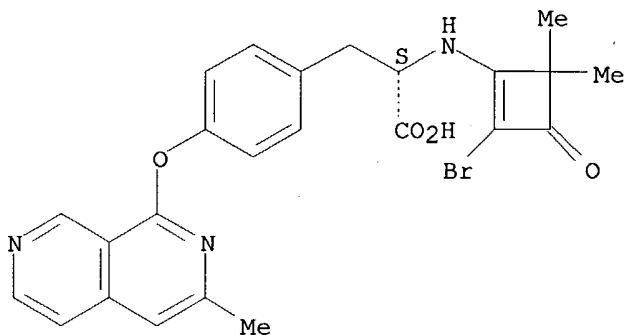


RN 455262-26-7 CAPLUS

CN L-Tyrosine, N-(2-hexyl-4,4-dimethyl-3-oxo-1-cyclobuten-1-yl)-O-2,7-naphthyridin-1-yl-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

10/081,072



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 5 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:408639 CAPLUS

DOCUMENT NUMBER: 136:401746

TITLE: Preparation of 3-substituted 2,7-naphthyridin-1-yl derivatives of squaric acid amides as selective α 4 integrin inhibitors

INVENTOR(S): Head, John Clifford; McKay, Catherine; Porter, John Robert

PATENT ASSIGNEE(S): Celltech R & D Limited, UK

SOURCE: PCT Int. Appl., 63 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

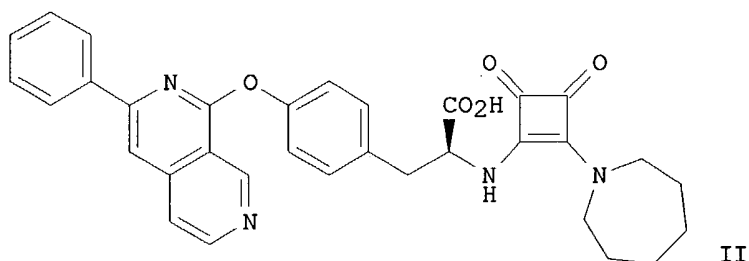
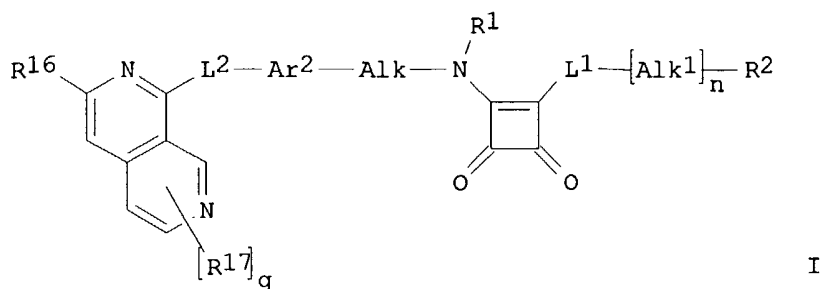
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002042264	A1	20020530	WO 2001-GB5168	20011122
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 2002018400	A5	20020603	AU 2002-18400	20011122
EP 1337534	A1	20030827	EP 2001-997474	20011122
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
US 2002137935	A1	20020926	US 2001-994411	20011127
US 6593338	B2	20030715		

PRIORITY APPLN. INFO.: GB 2000-28844 A 20001127
WO 2001-GB5168 W 20011122

OTHER SOURCE(S): MARPAT 136:401746

GI



AB The title compds. [I; R1 = H, alkyl; L1, L2 = a covalent bond, a linker atom or group; Alk1 = (un)substituted aliphatic chain; n = 0-1; R2 = H; (un)substituted heteroaliph., cycloaliph., heterocycloaliph., polycycloaliph., heteropolycycloaliph., aromatic or heteroarom. group; Alk = CH2CHR, CH:CR; CH(CH2R), C(:CHR) (wherein R = CO2H or a derivative or biostere thereof); Ar2 = (un)substituted aromatic or heteroarom. linking group; R16 = L3(Alk2)tL4R20 (L3, L4 = a covalent bond, a linker atom or group; t = 0-1; Alk2 = (un)substituted aliphatic or heteroaliph. chain; R20 = (un)substituted aromatic or heteroarom. group); g = 0-4; R17 = H, halo, alkyl, etc.] which are able to inhibit the binding of integrins to their ligands and are of use in the prophylaxis and treatment of immune or inflammatory disorders or disorders involving the inappropriate growth or migration of cells, were prepared E.g., a multi-step synthesis of (S)-II was given. The exemplified compds. I showed IC50 of $\leq 1 \mu\text{M}$ in the $\alpha 4\beta 1$ and $\alpha 4\beta 7$ assays.

IT **431038-15-2P 431038-16-3P**

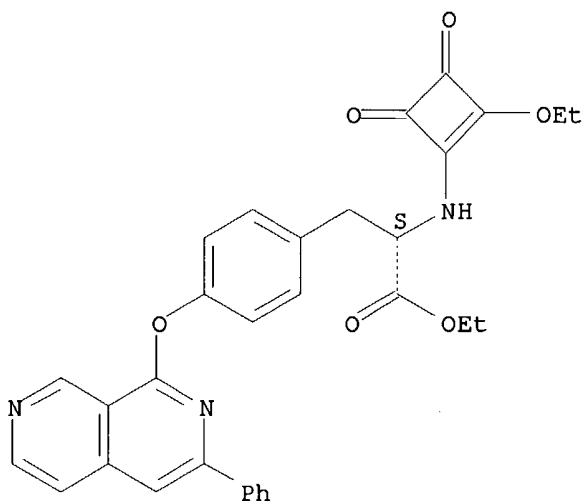
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 3-substituted 2,7-naphthyridin-1-yl derivs. of squaric acid amides as selective $\alpha 4$ integrin inhibitors)

RN 431038-15-2 CAPLUS

CN L-Tyrosine, N-(2-ethoxy-3,4-dioxo-1-cyclobuten-1-yl)-O-(3-phenyl-2,7-naphthyridin-1-yl)-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

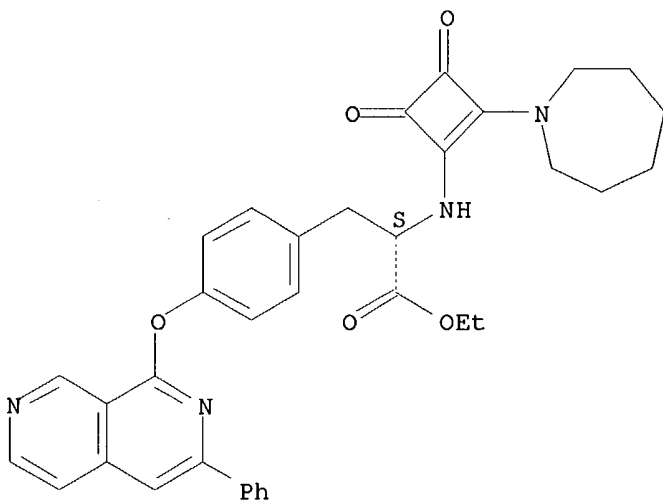
10/081,072



RN 431038-16-3 CAPLUS

CN L-Tyrosine, N-[2-(hexahydro-1H-azepin-1-yl)-3,4-dioxo-1-cyclobuten-1-yl]-O-(3-phenyl-2,7-naphthyridin-1-yl)-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 431038-17-4P

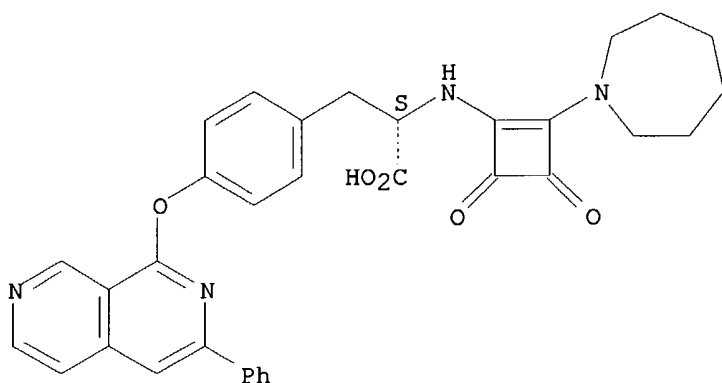
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 3-substituted 2,7-naphthyridin-1-yl derivs. of squaric acid amides as selective $\alpha 4$ integrin inhibitors)

RN 431038-17-4 CAPLUS

CN L-Tyrosine, N-[2-(hexahydro-1H-azepin-1-yl)-3,4-dioxo-1-cyclobuten-1-yl]-O-(3-phenyl-2,7-naphthyridin-1-yl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:211229 CAPLUS

DOCUMENT NUMBER: 137:210402

TITLE: Squaric acid derivatives as VLA-4 integrin antagonists

AUTHOR(S): Porter, John R.; Archibald, Sarah C.; Childs, Kirstie; Critchley, David; Head, John C.; Linsley, Janeen M.; Parton, Ted A. H.; Robinson, Martyn K.; Shock, Anthony; Taylor, Richard J.; Warrellow, Graham J.; Alexander, Rikki P.; Langham, Barry

CORPORATE SOURCE: Celltech R&D Ltd., Slough, SL1 4EN, UK

SOURCE: Bioorganic & Medicinal Chemistry Letters (2002), 12(7), 1051-1054

CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB SAR studies aimed at improving the rate of clearance by the incorporation of a 3,4-diamino-3-cyclobutene-1,2-dione group as an amino acid isostere in a series of VLA-4 integrin antagonists are described.

IT 312292-16-3P 312292-60-7P 312292-62-9P
312292-64-1P 312292-66-3P 312293-18-8P
312293-32-6P 312293-42-8P 312293-43-9P
312293-44-0P 312293-49-5P 312293-50-8P
312293-56-4P 312293-57-5P 312293-58-6P
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312293-68-8P 312293-69-9P 312293-70-2P
312293-71-3P 312293-73-5P 312293-74-6P
312293-81-5P 312293-82-6P 312293-89-3P
312293-90-6P 312293-91-7P 312293-92-8P
312294-01-2P 312294-02-3P 348113-48-4P
348113-50-8P 348113-52-0P 348113-54-2P
455894-84-5P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

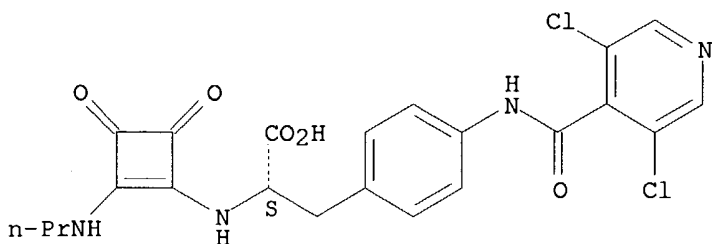
(squaric acid derivs. as VLA-4 integrin antagonists)

RN 312292-16-3 CAPLUS

CN L-Phenylalanine, 4-[[[(3,5-dichloro-4-pyridinyl)carbonyl]amino]-N-[3,4-dioxo-2-(propylamino)-1-cyclobuten-1-yl]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

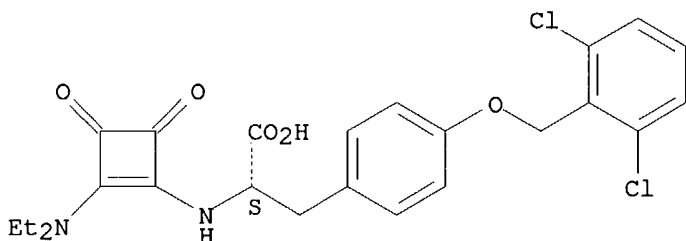
10/081,072



RN 312292-60-7 CAPLUS

CN L-Tyrosine, O-[(2,6-dichlorophenyl)methyl]-N-[2-(diethylamino)-3,4-dioxo-1-cyclobuten-1-yl]- (9CI) (CA INDEX NAME)

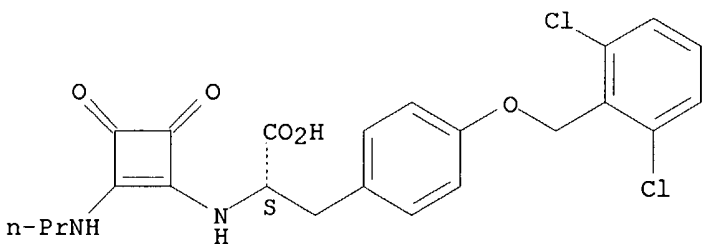
Absolute stereochemistry.



RN 312292-62-9 CAPLUS

CN L-Tyrosine, O-[(2,6-dichlorophenyl)methyl]-N-[3,4-dioxo-2-(propylamino)-1-cyclobuten-1-yl]- (9CI) (CA INDEX NAME)

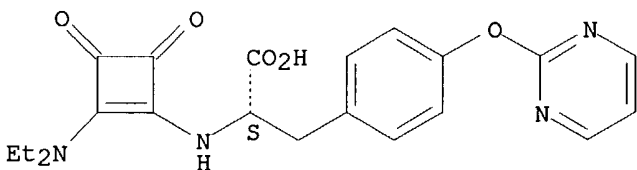
Absolute stereochemistry.



RN 312292-64-1 CAPLUS

CN L-Tyrosine, N-[2-(diethylamino)-3,4-dioxo-1-cyclobuten-1-yl]-O-2-pyrimidinyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

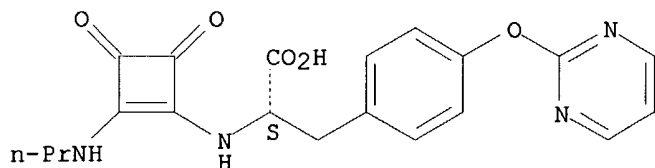


RN 312292-66-3 CAPLUS

10/081,072

CN L-Tyrosine, N-[3,4-dioxo-2-(propylamino)-1-cyclobuten-1-yl]-O-2-pyrimidinyl- (9CI) (CA INDEX NAME)

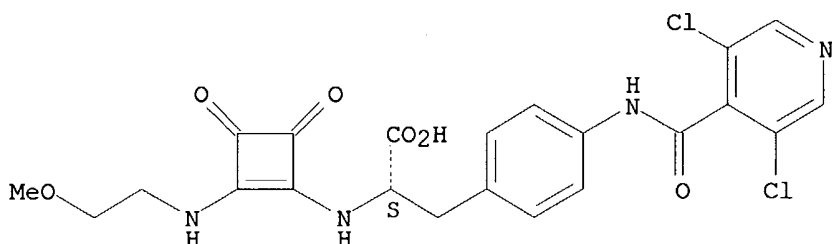
Absolute stereochemistry.



RN 312293-18-8 CAPLUS

CN L-Phenylalanine, 4-[[(3,5-dichloro-4-pyridinyl)carbonyl]amino]-N-[2-[(2-methoxyethyl)amino]-3,4-dioxo-1-cyclobuten-1-yl]- (9CI) (CA INDEX NAME)

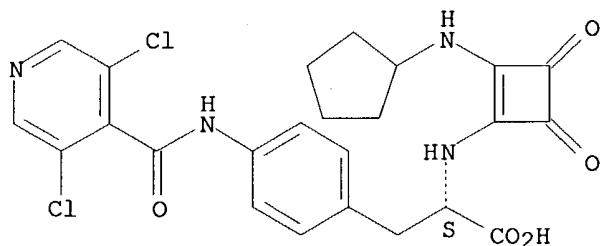
Absolute stereochemistry.



RN 312293-32-6 CAPLUS

CN L-Phenylalanine, N-[2-(cyclopentylamino)-3,4-dioxo-1-cyclobuten-1-yl]-4-[[(3,5-dichloro-4-pyridinyl)carbonyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 312293-42-8 CAPLUS

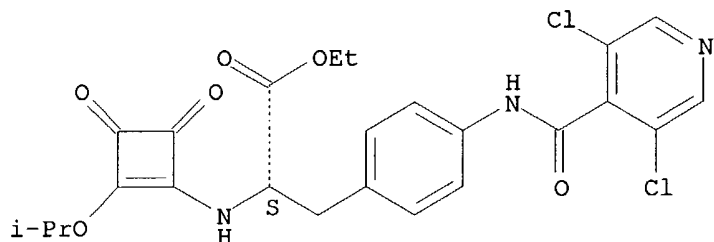
CN L-Phenylalanine, 4-[[(3,5-dichloro-4-pyridinyl)carbonyl]amino]-N-[2-[(1-methylethyl)amino]-3,4-dioxo-1-cyclobuten-1-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

10/081,072

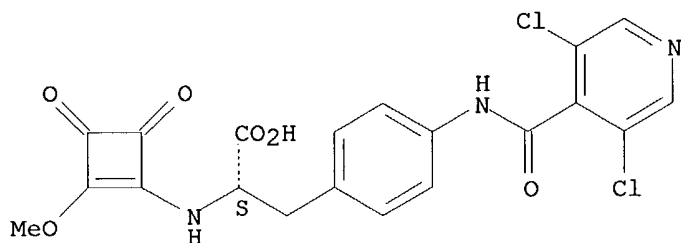
IT **312292-12-9P 312293-94-0DP**, resin-bound
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(squaric acid derivs. as VLA-4 integrin antagonists)
RN 312292-12-9 CAPLUS
CN L-Phenylalanine, 4-[[[(3,5-dichloro-4-pyridinyl)carbonyl]amino]-N-[2-(1-methylethoxy)-3,4-dioxo-1-cyclobuten-1-yl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 312293-94-0 CAPLUS
CN L-Phenylalanine, 4-[[[(3,5-dichloro-4-pyridinyl)carbonyl]amino]-N-(2-methoxy-3,4-dioxo-1-cyclobuten-1-yl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



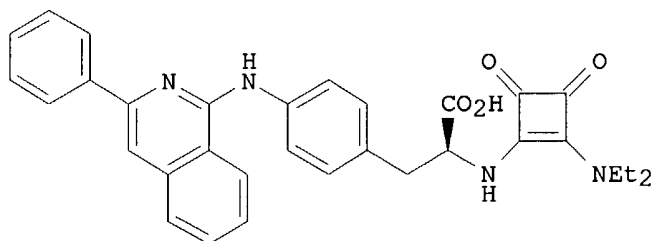
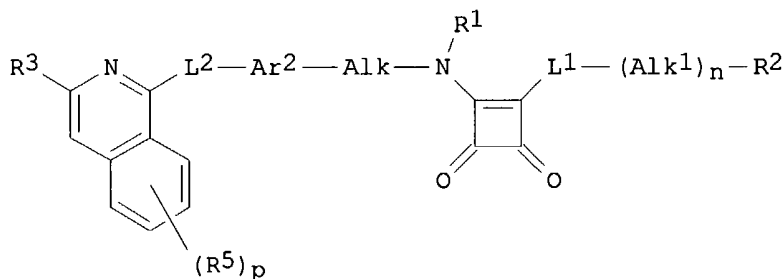
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:107317 CAPLUS
DOCUMENT NUMBER: 136:167287
TITLE: Preparation of novel 3-substituted isoquinolin-1-yl derivatives of squaric acid amides as selective α 4-integrin inhibitors
INVENTOR(S): Head, John Clifford; Porter, John Robert; McKay, Catherine
PATENT ASSIGNEE(S): Celltech R & D Limited, UK
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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10/081,072

WO 2002010136 A1 20020207 WO 2001-GB3429 20010730
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,
RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US,
UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
EP 1305291 A1 20030502 EP 2001-953234 20010730
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
JP 2004505110 T2 20040219 JP 2002-516268 20010730
US 6469025 B1 20021022 US 2001-920206 20010801
US 2002177605 A1 20021128
PRIORITY APPLN. INFO.: GB 2000-18969 A 20000802
 GB 2000-28837 A 20001127
 WO 2001-GB3429 W 20010730
OTHER SOURCE(S): MARPAT 136:167287
GI



AB Squaric acid derivs. I are described [wherein: R1 = H or C1-6 alkyl; L1 = covalent bond or linker atom or group; Alk1 = (un)substituted aliphatic chain; n = 0 or 1; R2 = H or (un)substituted heteroaliph., (hetero)cycloaliph., (hetero)polycycloaliph., (hetero)aromatic; Alk = CH2CH(R), CH:C(R), CH(CH2R), C(:CHR); R = CO2H or derivative or biostere thereof; Ar2 = (un)substituted (hetero)aromatic linker; L2 = covalent bond or linker atom or group; R3 = L3(Alk2)mL4R4; L3, L4 = covalent bond or linker atom or group; m = 0 or 1; Alk2 = (un)substituted (hetero)aliphatic chain; R4 = (un)substituted (hetero)aromatic group; p = 0-5; R5 = H, halo, (un)substituted alkyl, alkoxy, (hetero)aromatic, SH, OH, (un)substituted NH2, etc.; including salts, solvates, hydrates, and N-oxides]. The compds. are

able to inhibit the binding of integrins to their ligands and are of use in the prophylaxis and treatment of immune or inflammatory disorders, or disorders including the inappropriate growth or migration of cells. In particular, the compds. are selective inhibitors of $\alpha 4$ integrins. Approx. 50 compds. I were prepared For instance, mono-amidation of the squarate diester 3,4-diisopropoxy-3-cyclobutene-1,2-dione with a corresponding amino acid ester (84%), followed by a second amidation with diethylamine (85%), and alkaline hydrolysis of the ester function (67%), gave title compound II. In bioassays against several integrins, the example compds. generally had IC50 values of $\leq 1 \mu\text{M}$ against $\alpha 4\beta 1$ and $\alpha 4\beta 7$ integrins, but $\text{IC}_{50} \geq 50 \mu\text{M}$ against $\alpha 5\beta 1$, $\alpha \text{M}\beta 2$, and $\alpha \text{IIb}\beta 3$ integrins.

IT **395092-68-9P**, Ethyl (S)-2-[(2-isopropoxy-3,4-dioxocyclobuten-1-yl)amino]-3-[4-[(3-phenyl-1-isoquinolinyl)amino]phenyl]propanoate
395092-70-3P, Methyl (S)-2-[[2-(N,N-diethylamino)-3,4-dioxocyclobuten-1-yl]amino]-3-[4-[(3-phenyl-1-isoquinolinyl)amino]phenyl]propanoate **395092-71-4P**, (S)-2-[[2-(N,N-Diethylamino)-3,4-dioxocyclobuten-1-yl]amino]-3-[4-[(3-phenyl-1-isoquinolinyl)amino]phenyl]propanoic acid **395092-73-6P**, Methyl (S)-2-[[2-(N,N-dipropylamino)-3,4-dioxocyclobuten-1-yl]amino]-3-[4-[(3-phenyl-1-isoquinolinyl)amino]phenyl]propanoate **395092-75-8P**, (S)-2-[[2-(N,N-Dipropylamino)-3,4-dioxocyclobuten-1-yl]amino]-3-[4-[(3-phenyl-1-isoquinolinyl)amino]phenyl]propanoic acid **395092-77-0P**, Methyl (2S)-2-[[2-(2,5-dimethylpyrrolidin-1-yl)-3,4-dioxocyclobuten-1-yl]amino]-3-[4-[(3-phenyl-1-isoquinolinyl)amino]phenyl]propanoate **395092-78-1P**, (2S)-2-[[2-(2,5-Dimethylpyrrolidin-1-yl)-3,4-dioxocyclobuten-1-yl]amino]-3-[4-[(3-phenyl-1-isoquinolinyl)amino]phenyl]propanoic acid **395092-79-2P**, Ethyl (S)-2-[(2-isopropoxy-3,4-dioxocyclobuten-1-yl)amino]-3-[4-[(3-(4-fluorophenyl)-1-isoquinolinyl)amino]phenyl]propionate **395092-81-6P**, Ethyl (2S)-2-[[2-(2,5-dimethylpyrrolidin-1-yl)-3,4-dioxocyclobut-1-enyl]amino]-3-[4-[(3-(4-fluorophenyl)isoquinolin-1-yl)amino]phenyl]propanoate **395092-82-7P**, (2S)-2-[[2-(2,5-Dimethylpyrrolidin-1-yl)-3,4-dioxocyclobuten-1-yl]amino]-3-[4-[(3-(4-fluorophenyl)isoquinolin-1-yl)amino]phenyl]propanoic acid **395092-83-8P**, Ethyl (2S)-2-[[2-(2-methylpiperidin-1-yl)-3,4-dioxocyclobut-1-enyl]amino]-3-[4-[(3-(4-fluorophenyl)isoquinolin-1-yl)amino]phenyl]propanoate **395092-84-9P**, (2S)-2-[[2-(2-Methylpiperidin-1-yl)-3,4-dioxocyclobut-1-enyl]amino]-3-[4-[(3-(4-fluorophenyl)isoquinolin-1-yl)amino]phenyl]propanoic acid **395092-86-1P**, (2S)-3-[4-(3-Phenyl-1-isoquinolinylamino)phenyl]-2-(2-morpholino-3,4-dioxocyclobut-1-enylamino)propanoic acid **395092-87-2P**, (2S)-2-[[2-(Isobutylamino)-3,4-dioxocyclobut-1-enyl]amino]-3-[4-[(3-phenyl-1-isoquinolinyl)amino]phenyl]propanoic acid **395092-88-3P**, (2S)-2-[[2-[(2-Methoxyethyl)amino]-3,4-dioxocyclobut-1-enyl]amino]-3-[4-[(3-phenyl-1-isoquinolinyl)amino]phenyl]propanoic acid **395092-89-4P**, (2S)-2-[[2-(2-Ethylpiperidin-1-yl)-3,4-dioxocyclobut-1-enyl]amino]-3-[4-[(3-phenyl-1-isoquinolinyl)amino]phenyl]propanoic acid **395092-90-7P**, (2S)-2-[[2-(2-Propylpiperidin-1-yl)-3,4-dioxocyclobut-1-enyl]amino]-3-[4-[(3-phenyl-1-isoquinolinyl)amino]phenyl]propanoic acid **395092-91-8P**, (2S)-2-[[2-(5-Ethyl-2-methylpiperidin-1-yl)-3,4-dioxocyclobut-1-enyl]amino]-3-[4-[(3-phenyl-1-isoquinolinyl)amino]phenyl]propanoic acid **395092-92-9P**, (2S)-2-[[2-[(2R,5R)-2,5-Bis(methoxymethyl)pyrrolidin-1-yl]-3,4-dioxocyclobut-1-enyl]amino]-3-[4-[(3-phenyl-1-isoquinolinyl)amino]phenyl]propanoic acid **395092-93-0P**, (2S)-2-[[2-(Propylamino)-3,4-dioxocyclobut-1-enyl]amino]-3-[4-[(3-phenyl-1-isoquinolinyl)amino]phenyl]propanoic acid **395092-94-1P**, (S)-3-[4-[(3-Phenyl-1-isoquinolinyl)amino]phenyl]-2-[[2-(N-isopropyl-N-ethylamino)-3,4-dioxocyclobut-1-enyl]amino]propanoic acid

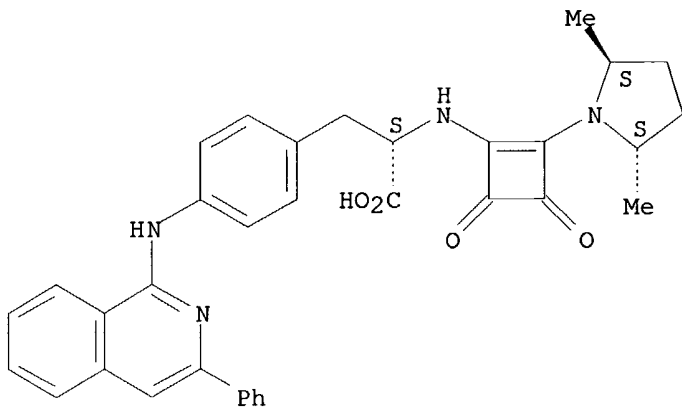
395092-95-2P, (2S)-2-[[2-(Diisobutylamino)-3,4-dioxocyclobut-1-enyl]amino]-3-[4-[(3-phenyl-1-isoquinolinyl)amino]phenyl]propanoic acid
395092-96-3P, (2S)-2-[[2-[(2R)-2-(Methoxymethyl)pyrrolidin-1-yl]-3,4-dioxocyclobut-1-enyl]amino]-3-[4-[(3-phenyl-1-isoquinolinyl)amino]phenyl]propanoic acid **395092-98-5P**, (S)-3-[4-[(3-Phenyl-1-isoquinolinyl)amino]phenyl]-2-[[2-(N-cyclohexyl-N-ethylamino)-3,4-dioxocyclobut-1-enyl]amino]propanoic acid
395092-99-6P, (2S)-2-[[2-(Piperidin-1-yl)-3,4-dioxocyclobut-1-enyl]amino]-3-[4-[(3-phenyl-1-isoquinolinyl)amino]phenyl]propanoic acid
395093-00-2P, (2S)-2-[[2-[2,5-Bis(2-methoxyethyl)amino]-3,4-dioxocyclobut-1-enyl]amino]-3-[4-[(3-phenyl-1-isoquinolinyl)amino]phenyl]propanoic acid **395093-01-3P**, (2S)-2-[[2-(3-Methylpiperidin-1-yl)-3,4-dioxocyclobut-1-enyl]amino]-3-[4-[(3-phenyl-1-isoquinolinyl)amino]phenyl]propanoic acid
395093-02-4P, (2S)-2-[[2-(Dibutylamino)-3,4-dioxocyclobut-1-enyl]amino]-3-[4-[(3-phenyl-1-isoquinolinyl)amino]phenyl]propanoic acid
395093-03-5P, (2S)-2-[[2-[2-(Pyridin-3-yl)pyrrolidin-1-yl]-3,4-dioxocyclobut-1-enyl]amino]-3-[4-[(3-phenyl-1-isoquinolinyl)amino]phenyl]propanoic acid **395093-04-6P**, (2S)-2-[[2-[Ethyl(pyridin-4-ylmethyl)amino]-3,4-dioxocyclobut-1-enyl]amino]-3-[4-[(3-phenyl-1-isoquinolinyl)amino]phenyl]propanoic acid
395093-05-7P 395093-07-9P, (2S)-2-[[2-(Decahydroquinolin-1-yl)-3,4-dioxocyclobut-1-enyl]amino]-3-[4-[(3-phenyl-1-isoquinolinyl)amino]phenyl]propanoic acid **395093-08-0P**, (2S)-2-[[2-[Methyl[(α S)- α -methylbenzyl]amino]-3,4-dioxocyclobut-1-enyl]amino]-3-[4-[(3-phenyl-1-isoquinolinyl)amino]phenyl]propanoic acid **395093-10-4P**, (S)-3-[4-[(3-Phenyl-1-isoquinolinyl)amino]phenyl]-2-[(2-(azepan-1-yl)-3,4-dioxocyclobut-1-enyl)amino]propanoic acid **395093-11-5P**, (2S)-2-[[2-(Thiomorpholin-4-yl)-3,4-dioxocyclobut-1-enyl]amino]-3-[4-[(3-phenyl-1-isoquinolinyl)amino]phenyl]propanoic acid **395093-12-6P**, (2S)-2-[[2-(2,6-Dimethylmorpholin-4-yl)-3,4-dioxocyclobut-1-enyl]amino]-3-[4-[(3-phenyl-1-isoquinolinyl)amino]phenyl]propanoic acid
395093-13-7P, (2S)-2-[[2-(Cyclopropylamino)-3,4-dioxocyclobut-1-enyl]amino]-3-[4-[(3-phenyl-1-isoquinolinyl)amino]phenyl]propanoic acid
395093-16-0P, (S)-3-[4-[(3-Phenyl-1-isoquinolinyl)amino]phenyl]-2-[[2-(N-cyclopropylmethyl-N-propylamino)-3,4-dioxocyclobut-1-enyl]amino]propanoic acid **395093-17-1P**, (2S)-2-[[2-(Isopropylamino)-3,4-dioxocyclobut-1-enyl]amino]-3-[4-[(3-phenyl-1-isoquinolinyl)amino]phenyl]propanoic acid **395093-18-2P**, (2S)-2-[[2-(1,2,3,4-Tetrahydroisoquinolin-2-yl)-3,4-dioxocyclobut-1-enyl]amino]-3-[4-[(3-phenyl-1-isoquinolinyl)amino]phenyl]propanoic acid
395093-19-3P, (2S)-2-[[2-(N-Benzyl-N-isopropylamino)-3,4-dioxocyclobut-1-enyl]amino]-3-[4-[(3-phenyl-1-isoquinolinyl)amino]phenyl]propanoic acid **395093-21-7P**, (2S)-2-[[2-(4-Methylhomopiperazin-1-yl)-3,4-dioxocyclobut-1-enyl]amino]-3-[4-[(3-phenyl-1-isoquinolinyl)amino]phenyl]propanoic acid
395093-23-9P, (2S)-2-[[2-[4-(tert-Butoxycarbonyl)homopiperazin-1-yl]-3,4-dioxocyclobut-1-enyl]amino]-3-[4-[(3-phenyl-1-isoquinolinyl)amino]phenyl]propanoic acid **395093-24-0P**, (2S)-2-[[2-(Thiazolidin-3-yl)-3,4-dioxocyclobut-1-enyl]amino]-3-[4-[(3-phenyl-1-isoquinolinyl)amino]phenyl]propanoic acid **395093-25-1P**, (2S)-2-[[2-(N-Benzyl-N-ethylamino)-3,4-dioxocyclobut-1-enyl]amino]-3-[4-[(3-phenyl-1-isoquinolinyl)amino]phenyl]propanoic acid
395093-26-2P, (2S)-2-[[2-[(2S,5S)-2,5-Dimethylpyrrolidin-1-yl]-3,4-dioxocyclobut-1-enyl]amino]-3-[4-[(3-phenyl-1-isoquinolinyl)amino]phenyl]propanoic acid

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

10/081,072

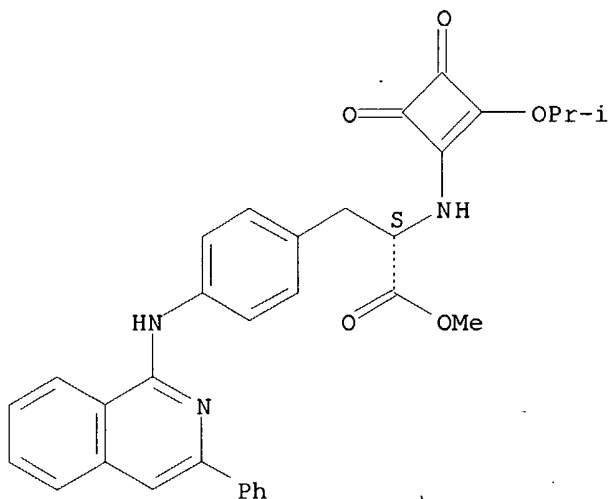
RN 395093-26-2 CAPLUS
CN L-Phenylalanine, N-[2-[(2S,5S)-2,5-dimethyl-1-pyrrolidiny]-3,4-dioxo-1-cyclobuten-1-yl]-4-[(3-phenyl-1-isoquinolinyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 395093-29-5, Methyl (S)-3-[4-(3-phenyl-1-isoquinolinylamino)phenyl]-2-(2-isopropoxy-3,4-dioxocyclobut-1-enylamino)propanoate
RL: RCT (Reactant); RACT (Reactant or reagent)
(precursor; preparation of 3-substituted isoquinolin-1-yl derivs. of squaric acid amides as α 4-integrin inhibitors)
RN 395093-29-5 CAPLUS
CN L-Phenylalanine, N-[2-(1-methylethoxy)-3,4-dioxo-1-cyclobuten-1-yl]-4-[(3-phenyl-1-isoquinolinyl)amino]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



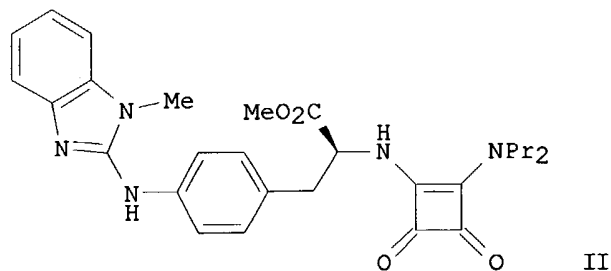
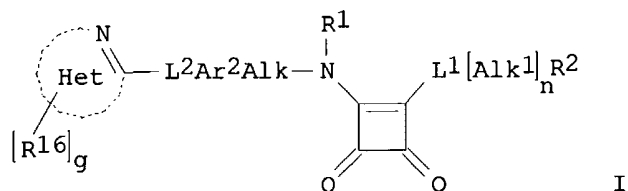
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:51439 CAPLUS

10/081,072

DOCUMENT NUMBER: 136:118460
TITLE: Preparation of squaric acid derivatives containing a bicyclic heteroaromatic ring as integrin antagonists
INVENTOR(S): Langham, Barry John; Alexander, Rikki Peter; Head, John Clifford; Linsley, Janeen Marsha; Porter, John Robert; Archibald, Sarah Catherine; Warrellow, Graham John
PATENT ASSIGNEE(S): Celltech R & D Limited, UK
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002004426	A1	20020117	WO 2001-GB3028	20010705
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002107263	A1	20020808	US 2001-899488	20010705
US 6740654	B2	20040525		
EP 1301488	A1	20030416	EP 2001-945540	20010705
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004502762	T2	20040129	JP 2002-509293	20010705
PRIORITY APPLN. INFO.:				
			GB 2000-16785	A 20000707
			GB 2000-28364	A 20001121
			WO 2001-GB3028	W 20010705
OTHER SOURCE(S): MARPAT 136:118460				
GI				



AB The title compds. [I; Het = (un)substituted bicyclic fused ring heteroarom. group; R16 = H, alkyl, etc.; g = 0-4; L2 = a bond, O, S, CO, etc.; Ar2 = (un)substituted (hetero)aromatic; Alk = CH₂CHR, CH:CR, CH(CH₂R), C(:CHR) (wherein R = CO₂H or a derivative or biostere thereof); R1 = H, alkyl; L1 = a covalent bond, a linker atom or group; Alk1 = (un)substituted aliphatic chain; n = 0-1; R2 = H, (un)substituted heteroaliph., cycloaliph., heterocycloaliph., polycycloaliphatic, heteropolycycloaliph., aromatic or heteroarom. group other than a 2,6-naphthyridin-1-yl, isoquinolin-1-yl, 2,7-naphthyridin-1-yl or quinazolin-4-yl] which are able to inhibit the binding of integrins to their ligands and are of use in the prophylaxis and treatment of immune or inflammatory disorders, or disorders involving the inappropriate growth or migration of cells, were prepared Thus, reacting Et (S)-2-amino-3-{4-[(1-methylbenzimidazol-2-yl)amino]phenyl}propanoate.CF₃CO₂H with diisopropylsquarate in the presence of DIPEA in iso-Pr followed by treatment of the resulting Et (S)-2-{[2-(isopropoxy)-3,4-dioxo-1-cyclobutenyl]amino}-3-{4-[(1-methylbenzimidazol-2-yl)amino]phenyl}propanoate with dipropylamine in MeOH afforded II. The exemplified compds. I showed IC₅₀ of $\leq 1 \mu\text{M}$ in the $\alpha 4\beta 1$ and $\alpha 4\beta 7$ assays.

IT 389637-00-7P 389637-01-8P 389637-02-9P

389637-06-3P 389637-07-4P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of squaric acid derivs. containing a bicyclic heteroarom. ring

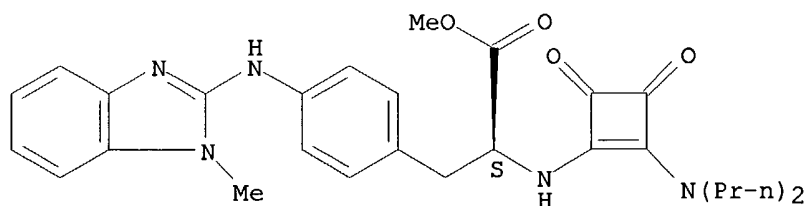
as

integrin antagonists)

RN 389637-00-7 CAPLUS

CN L-Phenylalanine, N-[2-(dipropylamino)-3,4-dioxo-1-cyclobuten-1-yl]-4-[(1-methyl-1H-benzimidazol-2-yl)amino]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

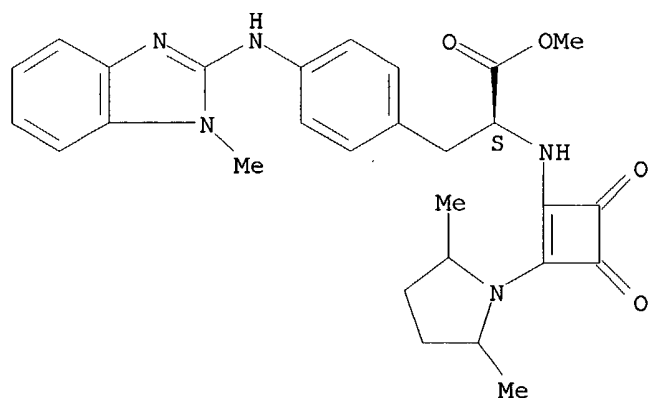


RN 389637-01-8 CAPLUS

CN L-Phenylalanine, N-[2-(2,5-dimethyl-1-pyrrolidinyl)-3,4-dioxo-1-cyclobuten-1-yl]-4-[(1-methyl-1H-benzimidazol-2-yl)amino]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

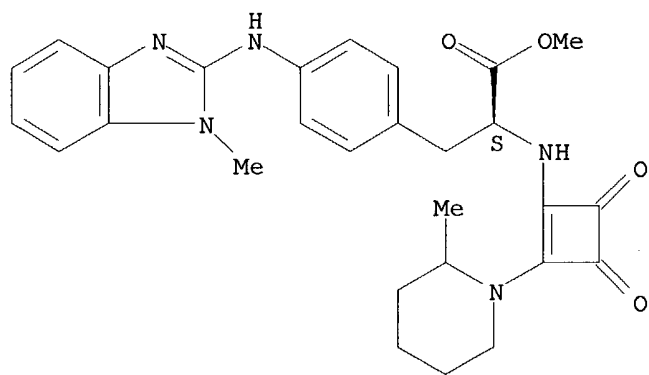
10/081,072



RN 389637-02-9 CAPLUS

CN L-Phenylalanine, 4-[(1-methyl-1H-benzimidazol-2-yl)amino]-N-[2-(2-methyl-1-piperidiny)-3,4-dioxo-1-cyclobuten-1-yl]-, methyl ester (9CI) (CA INDEX NAME)

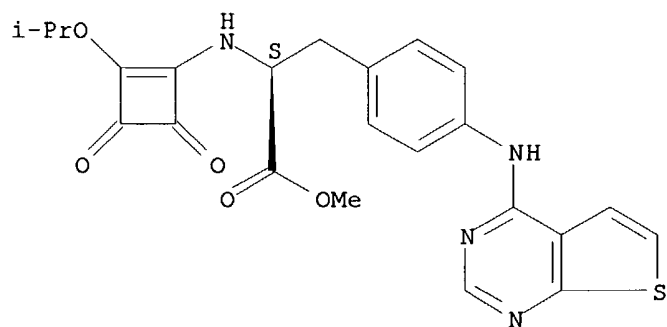
Absolute stereochemistry.



RN 389637-06-3 CAPLUS

CN L-Phenylalanine, N-[2-(1-methylethoxy)-3,4-dioxo-1-cyclobuten-1-yl]-4-(thieno[2,3-d]pyrimidin-4-ylamino)-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



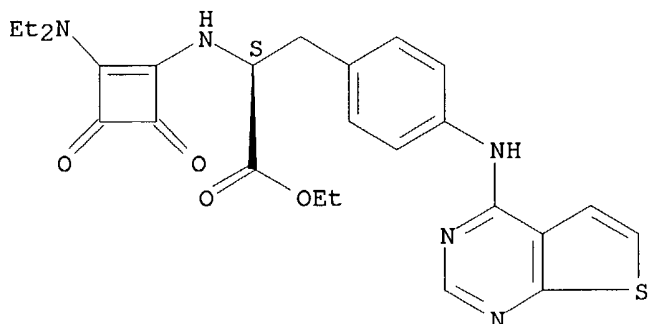
RN 389637-07-4 CAPLUS

CN L-Phenylalanine, N-[2-(diethylamino)-3,4-dioxo-1-cyclobuten-1-yl]-4-

10/081,072

(thieno[2,3-d]pyrimidin-4-ylamino)-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 389637-03-0P 389637-04-1P 389637-05-2P
389637-08-5P

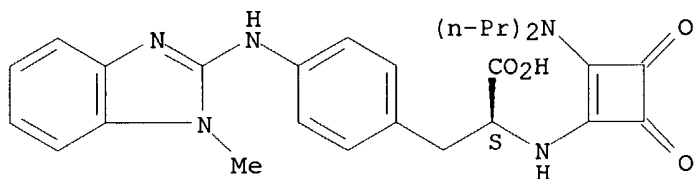
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)

(preparation of squaric acid derivs. containing a bicyclic heteroarom. ring
as integrin antagonists)

RN 389637-03-0 CAPLUS

CN L-Phenylalanine, N-[2-(dipropylamino)-3,4-dioxo-1-cyclobuten-1-yl]-4-[(1-methyl-1H-benzimidazol-2-yl)amino]- (9CI) (CA INDEX NAME)

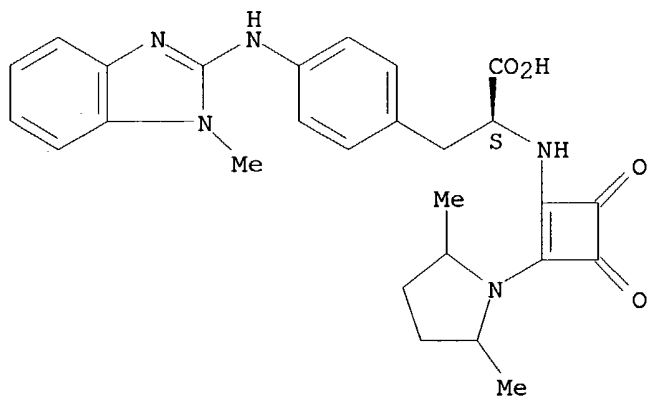
Absolute stereochemistry.



RN 389637-04-1 CAPLUS

CN L-Phenylalanine, N-[2-(2,5-dimethyl-1-pyrrolidinyl)-3,4-dioxo-1-cyclobuten-1-yl]-4-[(1-methyl-1H-benzimidazol-2-yl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

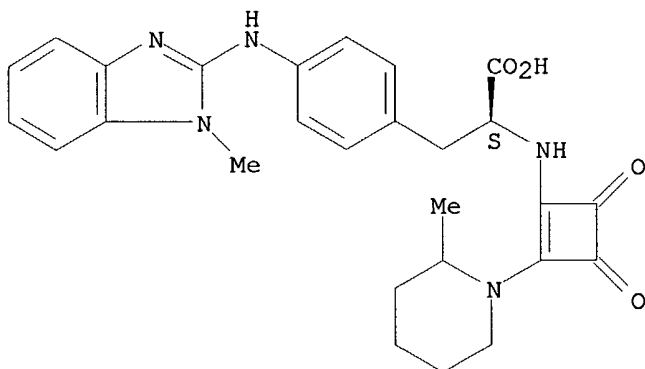


10/081,072

RN 389637-05-2 CAPLUS

CN L-Phenylalanine, 4-[(1-methyl-1H-benzimidazol-2-yl)amino]-N-[2-(2-methyl-1-piperidiny)-3,4-dioxo-1-cyclobuten-1-yl]- (9CI) (CA INDEX NAME)

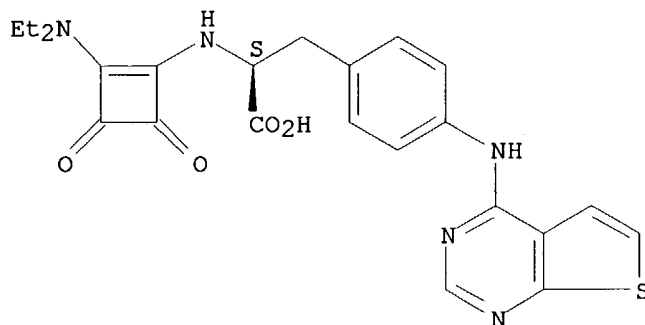
Absolute stereochemistry.



RN 389637-08-5 CAPLUS

CN L-Phenylalanine, N-[2-(diethylamino)-3,4-dioxo-1-cyclobuten-1-yl]-4-(thieno[2,3-d]pyrimidin-4-ylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 389637-11-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of squaric acid derivs. containing a bicyclic heteroarom. ring

as

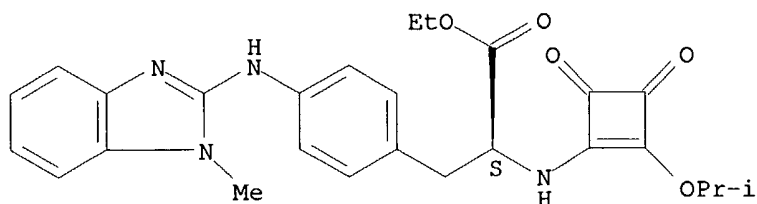
integrin antagonists)

RN 389637-11-0 CAPLUS

CN L-Phenylalanine, 4-[(1-methyl-1H-benzimidazol-2-yl)amino]-N-[2-(1-methylethoxy)-3,4-dioxo-1-cyclobuten-1-yl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

10/081,072



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:886114 CAPLUS

DOCUMENT NUMBER: 136:20059

TITLE: Preparation of naphthyridine squaric acid derivatives as integrin inhibitors.

INVENTOR(S): Langham, Barry John; Alexander, Rikki Peter; Head, John Clifford; Linsley, Janeen Marsha; Porter, John Robert; Archibald, Sarah Catherine; Warrellow, Graham John

PATENT ASSIGNEE(S): Celltech R & D Limited, UK

SOURCE: PCT Int. Appl., 101 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

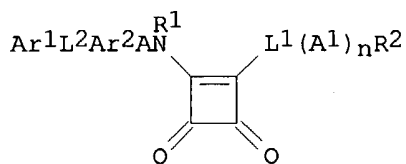
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001092256	A1	20011206	WO 2001-GB2425	20010530
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
US 2002115684	A1	20020822	US 2001-867016	20010529
US 6545013	B2	20030408		
EP 1286995	A1	20030305	EP 2001-934177	20010530
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
JP 2003535088	T2	20031125	JP 2002-500869	20010530
PRIORITY APPLN. INFO.:			GB 2000-13101	A 20000530
			GB 2000-28841	A 20001127
			WO 2001-GB2425	W 20010530

OTHER SOURCE(S): MARPAT 136:20059

GI



AB Title compds. [I; Ar¹ = (substituted) 2,7-naphthridin-1-yl; L² = bond, linker atom or group; Ar² = (substituted) aromatic or heteroarom. chain; A = CH₂CHR, CH:CR, CHCH₂R, C:CHR; R = CO₂H or a derivative or biostere thereof; R¹ = H, alkyl; L¹ = bond, linker atom or group; A¹ = (substituted) aliphatic chain; n = 0, 1; R² = H, (substituted) heteroaliph., cycloaliph., heterocycloaliph., polycycloaliph., heteropolycycloaliph., aryl, heteroaryl] and the salts, solvates, hydrates and N-oxides thereof, were prepared. Thus, a mixture of 1,2-diisopropoxy-3,4-dioxocyclobut-1-ene and Et (S)-3-[4-(2,7-naphthyridin-1-ylamino)phenyl]-2-aminopropanoate (preparation given) in EtOH was stirred at 50° overnight to give 79% Et (S)-3-[4-(2,7-naphthyridin-1-ylamino)phenyl]-2-(2-isopropoxy-3,4-dioxocyclobut-1-enylamino)propanoate. Tested I in α₄β₁ and α₄β₇ screens inhibited cell adhesion with IC₅₀ ≤ 1 μM.

IT 378251-41-3P 378251-42-4P 378251-43-5P
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378252-71-2P 378252-72-3P 378252-73-4P
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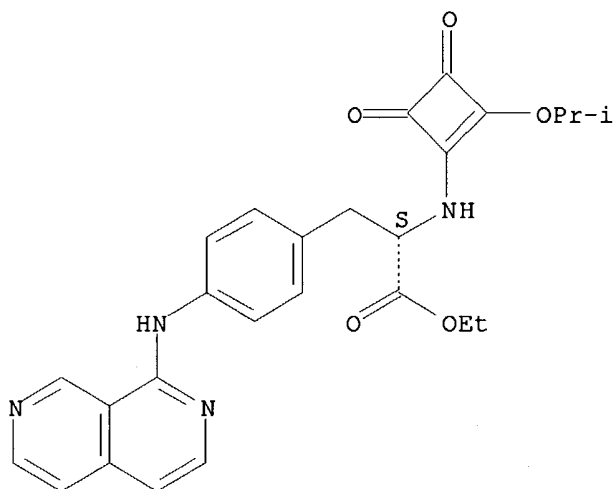
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)

(preparation of naphthyridine squaric acid derivs. as integrin inhibitors)

RN 378251-41-3 CAPLUS

CN L-Phenylalanine, N-[2-(1-methylethoxy)-3,4-dioxo-1-cyclobuten-1-yl]-4-(2,7-naphthyridin-1-ylamino)-, ethyl ester (9CI) (CA INDEX NAME)

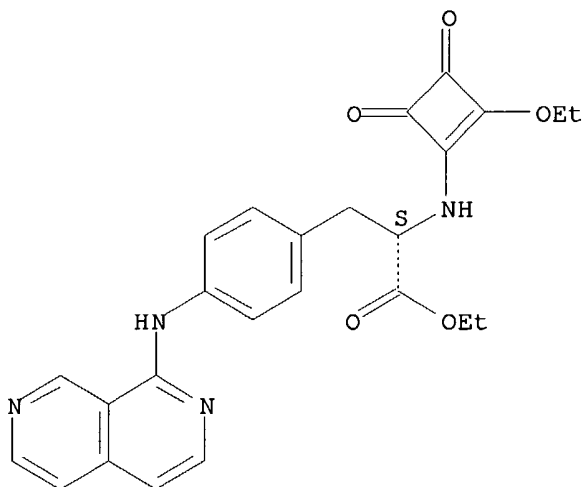
Absolute stereochemistry.



RN 378251-42-4 CAPLUS

CN L-Phenylalanine, N-(2-ethoxy-3,4-dioxo-1-cyclobuten-1-yl)-4-(2,7-naphthyridin-1-ylamino)-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 378251-43-5 CAPLUS

CN L-Phenylalanine, N-[2-(diethylamino)-3,4-dioxo-1-cyclobuten-1-yl]-4-(2,7-

10/081,072

L14 ANSWER 10 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:886077 CAPLUS

DOCUMENT NUMBER: 136:20029

TITLE: Preparation of squaric acid isoquinoline derivatives as integrin binding inhibitors.

INVENTOR(S): Langham, Barry John; Alexander, Rikki Peter; Head, John Clifford; Linsley, Janeen Marsha; Porter, John Robert; Archibald, Sarah Catherine; WarreLOW, Graham John

PATENT ASSIGNEE(S): Celltech R & D Limited, UK

SOURCE: PCT Int. Appl., 102 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

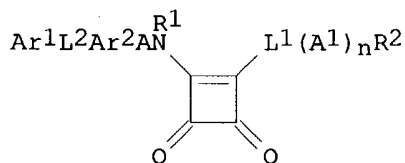
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001092233	A1	20011206	WO 2001-GB2390	20010530
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
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EP 1284967	A1	20030226	EP 2001-934158	20010530
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
JP 2003535081	T2	20031125	JP 2002-500847	20010530
PRIORITY APPLN. INFO.:			GB 2000-13087	A 20000530
			GB 2000-19060	A 20000803
			GB 2000-28842	A 20001127
			WO 2001-GB2390	W 20010530

OTHER SOURCE(S): MARPAT 136:20029

GI



AB Title compds. [I; Ar1 = 3-substituted isoquinolin-1-yl; L1, L2 = bond, linker atom or group; Ar2 = (substituted) aromatic or heteroanomatic chain; A = CH2CHR, CH:CR, CH(CH2R), C(:CHR); R = CO2H or a derivative or biostere thereof; R1 = H, alkyl; A1 = (substituted) aliphatic chain; n = 0, 1; R2 = H, (substituted) heteroaliph., cycloaliph., heterocycloaliph., polycycloaliph., heteropolycycloalkyl], were prepared as integrin binding inhibitors (no data). Thus, Me (S)-2-amino-3-[4-(3-ethyl-1-isoquinolinylamino)phenyl]propanoate (preparation given), 3,4-diisopropoxy-3-

cyclobuten-1,2-dione, and diisopropylethylamine were stirred 16 h in MeOH to give 100% Me (S)-3-[4-(3-ethyl-1-isoquinolinylamino)phenyl]-2-[(2-isopropoxy-3,4-dioxocyclobut-1-enyl)amino]propanoate. I generally show $IC_{50} \leq 1 \mu M$ in integrin $\alpha 4\beta 1$ and $\alpha 4\beta 7$ cell adhesion inhibition assays.

IT 378234-59-4P 378234-60-7P 378234-61-8P
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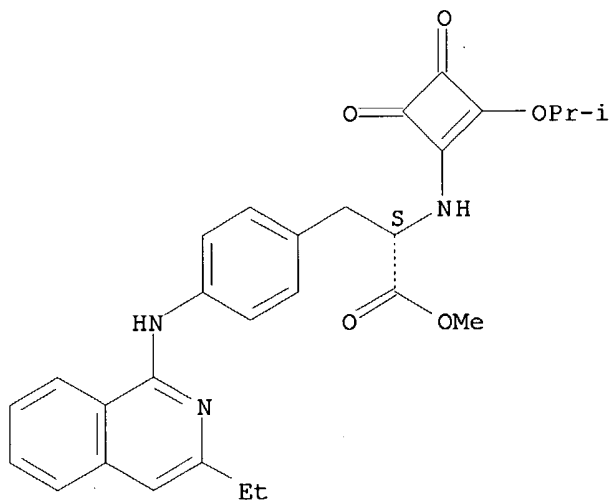
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of squaric acid isoquinoline derivs. as integrin binding inhibitors)

RN 378234-59-4 CAPLUS

CN L-Phenylalanine, 4-[(3-ethyl-1-isoquinolinyl)amino]-N-[2-(1-methylethoxy)-3,4-dioxo-1-cyclobuten-1-yl]-, methyl ester (9CI) (CA INDEX NAME)

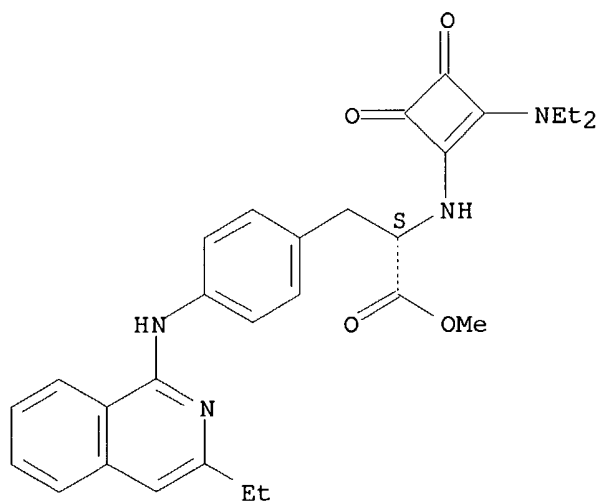
Absolute stereochemistry.



RN 378234-60-7 CAPLUS

CN L-Phenylalanine, N-[2-(diethylamino)-3,4-dioxo-1-cyclobuten-1-yl]-4-[(3-ethyl-1-isoquinolinyl)amino]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

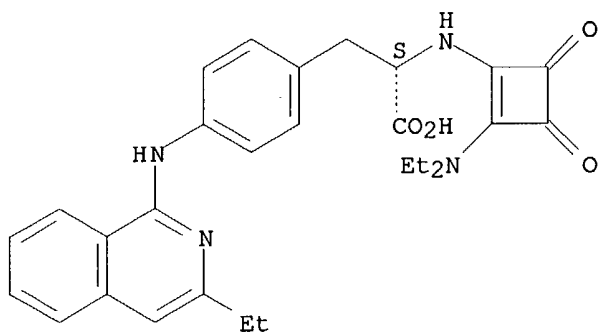


RN 378234-61-8 CAPLUS

CN L-Phenylalanine, N-[2-(diethylamino)-3,4-dioxo-1-cyclobuten-1-yl]-4-[(3-ethyl-1-isoquinolinyl)amino]- (9CI) (CA INDEX NAME)

10/081,072

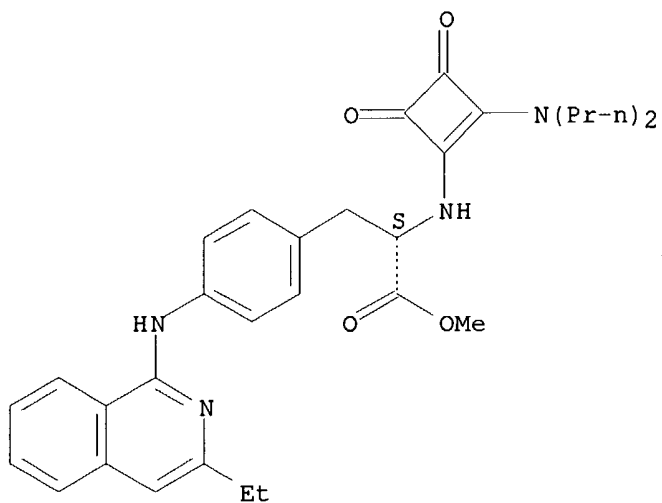
Absolute stereochemistry.



RN 378234-62-9 CAPLUS

CN L-Phenylalanine, N-[2-(dipropylamino)-3,4-dioxo-1-cyclobuten-1-yl]-4-[(3-ethyl-1-isoquinolinylnyl)amino]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

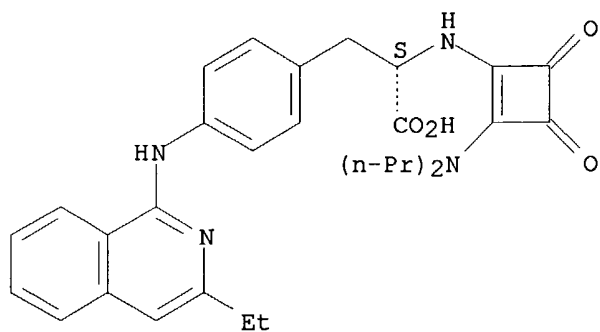


RN 378234-63-0 CAPLUS

CN L-Phenylalanine, N-[2-(dipropylamino)-3,4-dioxo-1-cyclobuten-1-yl]-4-[(3-ethyl-1-isoquinolinylnyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

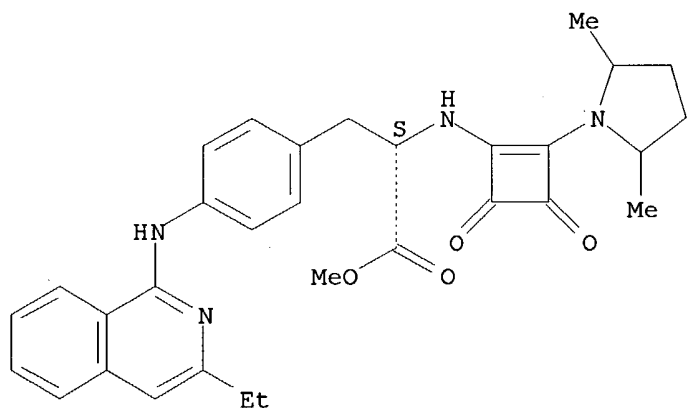
10/081,072



RN 378234-64-1 CAPLUS

CN L-Phenylalanine, N-[2-(2,5-dimethyl-1-pyrrolidinyl)-3,4-dioxo-1-cyclobuten-1-yl]-4-[(3-ethyl-1-isoquinolyl)amino]-, methyl ester (9CI) (CA INDEX NAME)

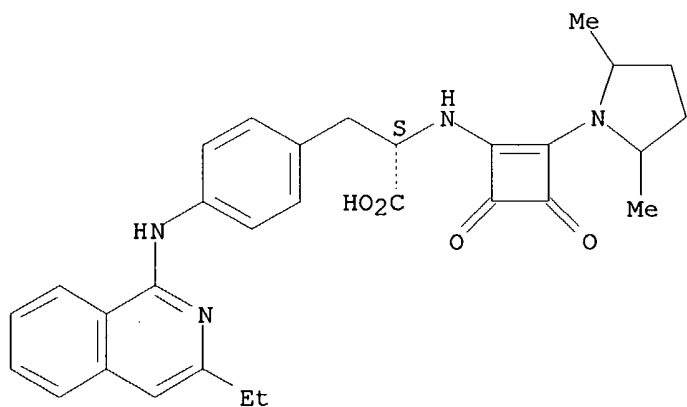
Absolute stereochemistry.



RN 378234-65-2 CAPLUS

CN L-Phenylalanine, N-[2-(2,5-dimethyl-1-pyrrolidinyl)-3,4-dioxo-1-cyclobuten-1-yl]-4-[(3-ethyl-1-isoquinolyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

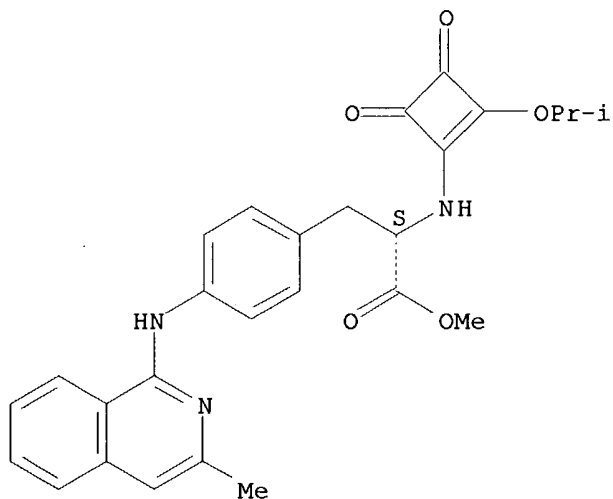


RN 378234-66-3 CAPLUS

10/081,072

CN L-Phenylalanine, N-[2-(1-methylethoxy)-3,4-dioxo-1-cyclobuten-1-yl]-4-[(3-methyl-1-isoquinolinyl)amino]-, methyl ester (9CI) (CA INDEX NAME)

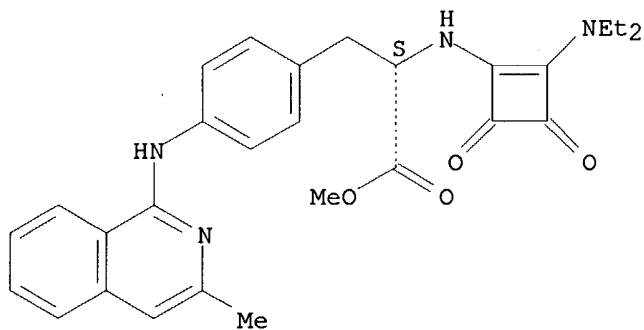
Absolute stereochemistry.



RN 378234-67-4 CAPLUS

CN L-Phenylalanine, N-[2-(diethylamino)-3,4-dioxo-1-cyclobuten-1-yl]-4-[(3-methyl-1-isoquinolinyl)amino]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

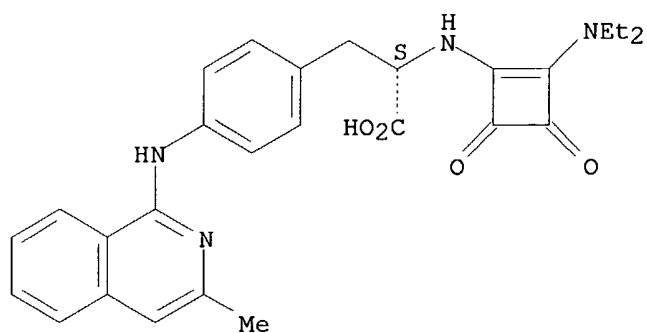


RN 378234-68-5 CAPLUS

CN L-Phenylalanine, N-[2-(diethylamino)-3,4-dioxo-1-cyclobuten-1-yl]-4-[(3-methyl-1-isoquinolinyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

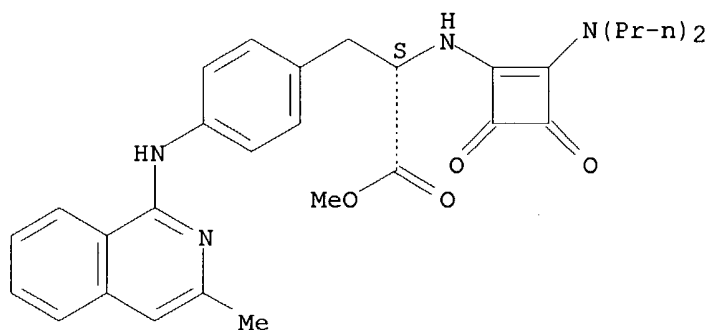
10/081,072



RN 378234-69-6 CAPLUS

CN L-Phenylalanine, N-[2-(dipropylamino)-3,4-dioxo-1-cyclobuten-1-yl]-4-[(3-methyl-1-isoquinolinyl)amino]-, methyl ester (9CI) (CA INDEX NAME)

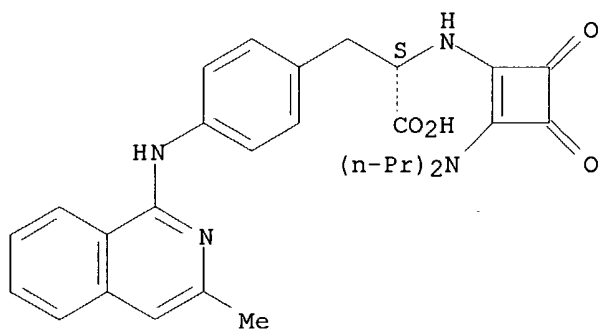
Absolute stereochemistry.



RN 378234-71-0 CAPLUS

CN L-Phenylalanine, N-[2-(dipropylamino)-3,4-dioxo-1-cyclobuten-1-yl]-4-[(3-methyl-1-isoquinolinyl)amino]- (9CI) (CA INDEX NAME)

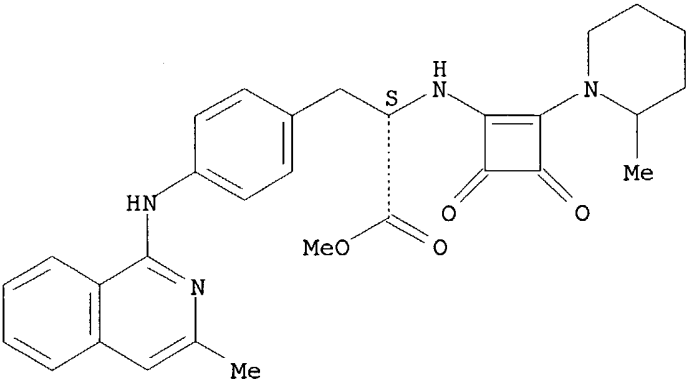
Absolute stereochemistry.



RN 378234-72-1 CAPLUS

CN L-Phenylalanine, 4-[(3-methyl-1-isoquinolinyl)amino]-N-[2-(2-methyl-1-piperidiny)-3,4-dioxo-1-cyclobuten-1-yl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 11 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:489353 CAPLUS

DOCUMENT NUMBER: 135:92389

TITLE: Preparation of squaric acid derivatives as integrin antagonists

INVENTOR(S): Langham, Barry John; Alexander, Rikki Peter; Head, John Clifford; Linsley, Janeen Marsha; Porter, John Robert; Archibald, Sarah Catherine; Warrellow, Graham John

PATENT ASSIGNEE(S): Celltech Chiroscience Limited, UK

SOURCE: PCT Int. Appl., 60 pp.

CODEN: PIXXD2

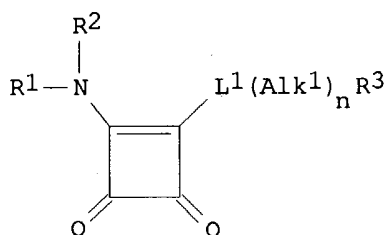
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001047867	A1	20010705	WO 2000-GB4995	20001222
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2001020017	A1	20010906	US 2000-742038	20001221
US 6455539	B2	20020924		
EP 1244611	A1	20021002	EP 2000-987574	20001222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRIORITY APPLN. INFO.:			GB 1999-30558	A 19991223
			GB 2000-2872	A 20000208
			GB 2000-28838	A 20001127
			WO 2000-GB4995	W 20001222
OTHER SOURCE(S):			CASREACT 135:92389; MARPAT 135:92389	
GI				



I

AB Preparation of squaric acid derivs. I are described (R1 = Ar1, Ar2Alk- in which Ar1 is an optionally substituted aromatic or heteroarom. group; Ar2 = optionally substituted phenylene or nitrogen-containing six-membered heteroarylene group; Alk = a chain -CH2CH(R)-, CH:C:C(R)-, (a) in which R is a carboxylic acid (-CO2H) or a derivative or biostere thereof; R2 = H, C1-6 alkyl; L1 = covalent bond or a linker atom or group; n = 0-1; Alk1 =

optionally substituted aliphatic chain; R3 = H, optionally substituted heteroaliph., cycloaliph., heterocycloaliph., polycycloaliph., heteropolycycloaliph., aromatic or heteroarom. group: and the salts, solvates, hydrates and N-oxides thereof). The compds. are able to inhibit the binding of integrins to their ligands and are of use in the prophylaxis and treatment of immune or inflammatory disorders, or disorders involving the inappropriate growth or migration of cells.

IT **348113-51-9P 348113-53-1P 348113-55-3P**

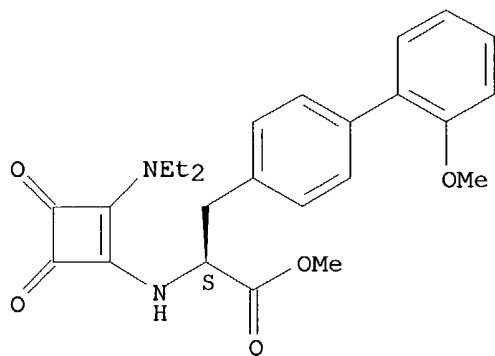
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of squaric acid derivs. as integrin antagonists)

RN 348113-51-9 CAPLUS

CN [1,1'-Biphenyl]-4-propanoic acid, α -[[2-(diethylamino)-3,4-dioxo-1-cyclobuten-1-yl]amino]-2'-methoxy-, methyl ester, (α S)- (9CI) (CA INDEX NAME)

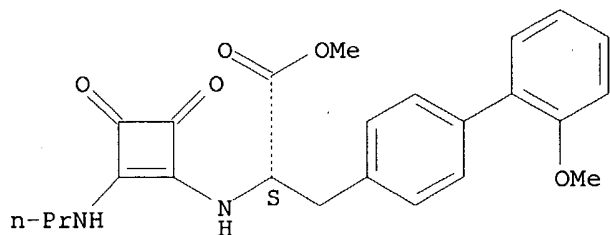
Absolute stereochemistry.



RN 348113-53-1 CAPLUS

CN [1,1'-Biphenyl]-4-propanoic acid, α -[[3,4-dioxo-2-(propylamino)-1-cyclobuten-1-yl]amino]-2'-methoxy-, methyl ester, (α S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

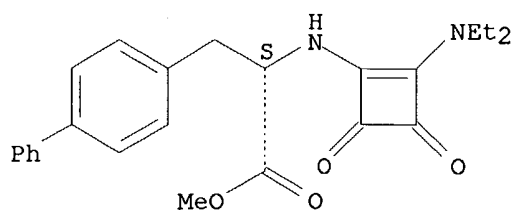


RN 348113-55-3 CAPLUS

CN [1,1'-Biphenyl]-4-propanoic acid, α -[[2-(diethylamino)-3,4-dioxo-1-cyclobuten-1-yl]amino]-, methyl ester, (α S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

10/081,072



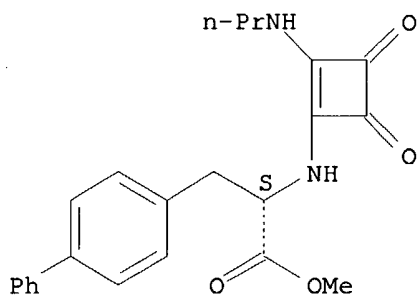
IT 348113-45-1P 348113-46-2P 348113-47-3P
348113-48-4P 348113-49-5P 348113-50-8P
348113-52-0P 348113-54-2P 348113-56-4P
348113-60-0P 348113-61-1P 348113-62-2P
348113-63-3P 348113-64-4P 348113-65-5P
348113-66-6P 348113-67-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of squaric acid derivs. as integrin antagonists)

RN 348113-45-1 CAPLUS

CN [1,1'-Biphenyl]-4-propanoic acid, α -[[3,4-dioxo-2-(propylamino)-1-cyclobuten-1-yl]amino]-, methyl ester, (α S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



10/081,072

ER 12 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:909217 CAPLUS

DOCUMENT NUMBER: 134:56962

TITLE: Preparation of 3,4-diamino-3-cyclobutene-1,2-dione derivatives which inhibit leukocyte adhesion mediated by VLA-4

INVENTOR(S): Lombardo, Louis J.; Sabalski, Joan

PATENT ASSIGNEE(S): American Home Products Corp., USA

SOURCE: U.S., 21 pp.

CODEN: USXXAM

DOCUMENT TYPE: Patent

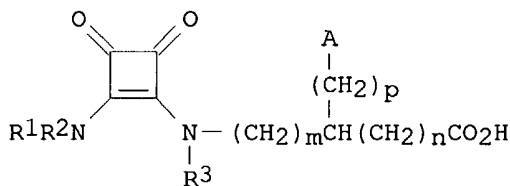
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6166050	A	20001226	US 1999-458852	19991210
PRIORITY APPLN. INFO.:			US 1998-155221P P	19981214
OTHER SOURCE(S):		MARPAT 134:56962		

GI



AB Diaminocyclobutenedione amino acid derivs. I (R1 = alkyl, aryl, heteroaryl, aralkyl, heteroaralkyl; R2 = H, alkyl, aryl, heteroaryl, aralkyl, heteroaralkyl or R1R2N form a saturated or unsatd. heterocyclic ring; R3 = H, alkyl, aryl, heteroaryl, aralkyl, heteroaralkyl; A = aryl, heteroaryl; m, n, p = 0-3) were prepared for the treatment of inflammatory and autoimmune diseases. Thus, N-[2-(benzylamino)-3,4-dioxocyclobut-1-enyl]-L-phenylalanine, prepared by treatment of L-phenylalanine Me ester hydrochloride with 3,4-diethoxy-3-cyclobutene-1,2-dione and benzylamine and saponification, showed IC50 = 58 μ M for binding of α 4 β 1 integrin (VLA-4).

IT 274927-11-6P 274927-14-9P 274927-20-7P
274927-22-9P 274927-24-1P 274927-26-3P
274927-29-6P 274927-31-0P 274927-33-2P
274927-38-7P 274927-51-4P 274927-53-6P
274927-56-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

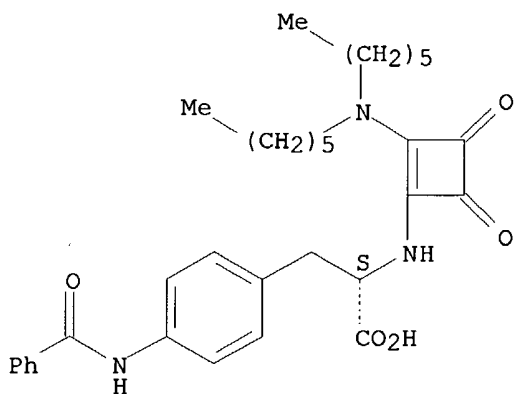
(preparation of diaminocyclobutenedione derivs. which inhibit leukocyte adhesion mediated by VLA-4)

RN 274927-11-6 CAPLUS

CN L-Phenylalanine, 4-(benzoylamino)-N-[2-(dihexylamino)-3,4-dioxo-1-cyclobuten-1-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

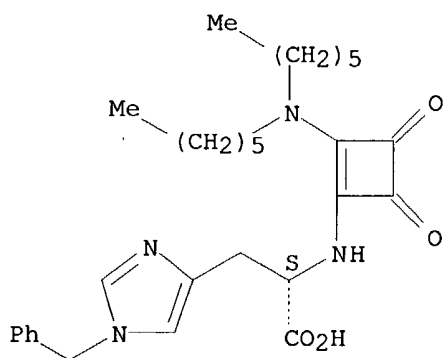
10/081,072



RN 274927-14-9 CAPLUS

CN L-Histidine, N-[2-(dihexylamino)-3,4-dioxo-1-cyclobuten-1-yl]-1-(phenylmethyl)- (9CI) (CA INDEX NAME)

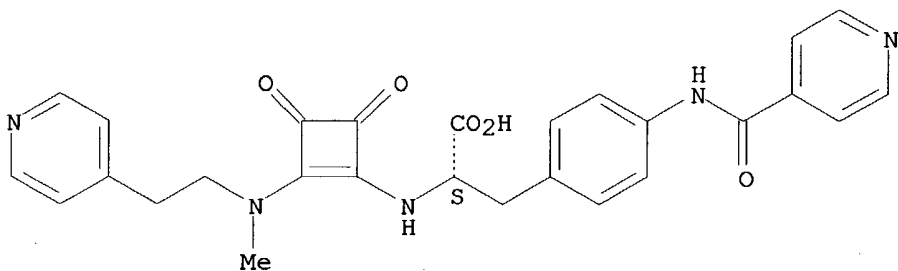
Absolute stereochemistry.



RN 274927-20-7 CAPLUS

CN L-Phenylalanine, N-[2-[methyl[2-(4-pyridinyl)ethyl]amino]-3,4-dioxo-1-cyclobuten-1-yl]-4-[(4-pyridinylcarbonyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

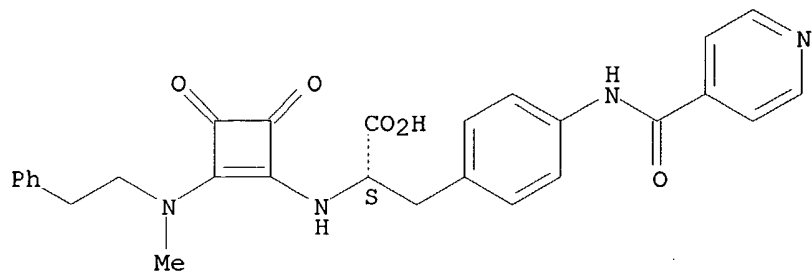


RN 274927-22-9 CAPLUS

CN L-Phenylalanine, N-[2-[methyl(2-phenylethyl)amino]-3,4-dioxo-1-cyclobuten-1-yl]-4-[(4-pyridinylcarbonyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

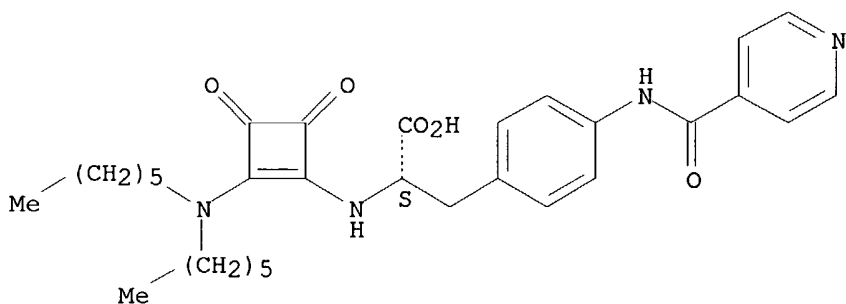
10/081,072



RN 274927-24-1 CAPLUS

CN L-Phenylalanine, N-[2-(dihexylamino)-3,4-dioxo-1-cyclobuten-1-yl]-4-[(4-pyridinylcarbonyl)amino]- (9CI) (CA INDEX NAME)

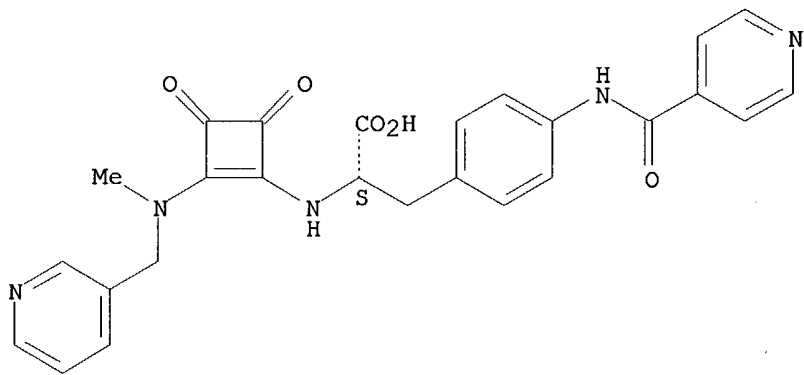
Absolute stereochemistry.



RN 274927-26-3 CAPLUS

CN L-Phenylalanine, N-[2-[methyl(3-pyridinylmethyl)amino]-3,4-dioxo-1-cyclobuten-1-yl]-4-[(4-pyridinylcarbonyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

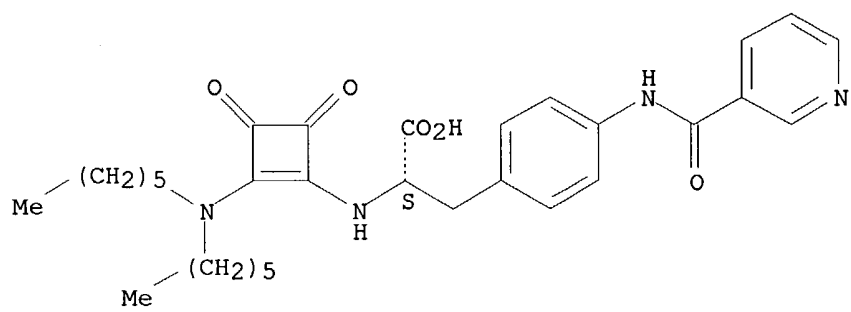


RN 274927-29-6 CAPLUS

CN L-Phenylalanine, N-[2-(dihexylamino)-3,4-dioxo-1-cyclobuten-1-yl]-4-[(3-pyridinylcarbonyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

10/081,072



10/081,072

L14 ANSWER 13 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:861644 CAPLUS

DOCUMENT NUMBER: 134:29705

TITLE: Preparation of squaric acid derivatives as cell adhesion molecules

INVENTOR(S): Langham, Barry John; Alexander, Rikki Peter; Head, John Clifford; Linsley, Janeen Marsha; Porter, John Robert; Archibald, Sarah Catherine; Warrelow, Graham John

PATENT ASSIGNEE(S): Celltech Chiroscience Limited, UK

SOURCE: PCT Int. Appl., 144 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

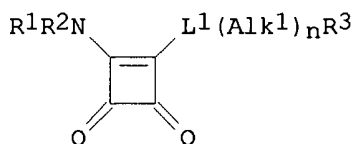
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000073260	A1	20001207	WO 2000-GB2020	20000526
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
US 6518283	B1	20030211	US 2000-579317	20000525
EP 1181266	A1	20020227	EP 2000-935341	20000526
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
JP 2003500467	T2	20030107	JP 2000-621327	20000526
US 2003162799	A1	20030828	US 2002-319272	20021213
PRIORITY APPLN. INFO.:			GB 1999-12640	A 19990528
			GB 2000-2858	A 20000208
			US 2000-579317	A3 20000525
			WO 2000-GB2020	W 20000526

OTHER SOURCE(S): MARPAT 134:29705

GI



AB Squaric acid derivs. I [R1 is an integrin binding group; R2 is a hydrogen atom or a C1-6 alkyl group; L1 is a covalent bond or a linker atom or group; n = 0, 1; Alk1 is an optionally substituted aliphatic chain; R3 is H or an optionally substituted heteroaliph., cycloaliph., heterocycloaliph., polycycloaliph., polyheterocycloaliph., aromatic or heteroarom. group] and their salts, solvates, hydrates and N-oxides were prepared as inhibitors of

the binding of integrins to their ligands. Thus, treatment of Et (S)-3-(4-aminophenyl)-2-(tert-butoxycarbonylamino)propionate with 3,5-dichloro-4-pyridinecarboxylic acid, deprotection, reaction with 3,4-diisopropoxy-3-cyclobutene-1,2-dione, propylation, and saponification afforded (S)-3-[4-(3,5-dichloro-4-pyridylcarboxamido)phenyl]-2-(2-propylamino-3,4-dioxocyclobut-1-enylamino)propanoic acid. Compds. of the invention in which R1 is an $\alpha 4$ integrin binding group generally have IC₅₀ values <1 μ M in the $\alpha 4\beta 1$ and $\alpha 4\beta 7$ assays.

IT **312292-12-9P**

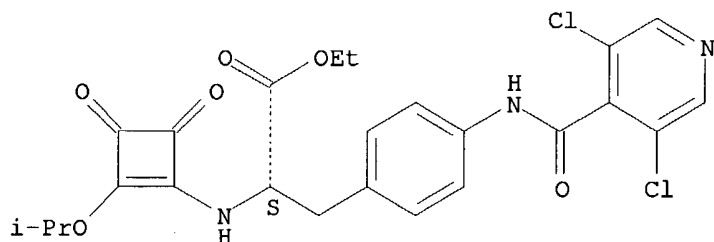
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(Preparation of squaric acid derivs. as cell adhesion mols.)

RN 312292-12-9 CAPLUS

CN L-Phenylalanine, 4-[[[(3,5-dichloro-4-pyridinyl)carbonyl]amino]-N-[2-(1-methylethoxy)-3,4-dioxo-1-cyclobuten-1-yl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **312292-13-0P 312292-15-2P 312292-17-4P**

312292-19-6P 312292-21-0P 312292-23-2P

312292-24-3P 312292-25-4P 312292-40-3P

312292-45-8P 312292-46-9P 312292-48-1P

312292-67-4P 312292-68-5P 312292-86-7P

312293-01-9P 312293-02-0P

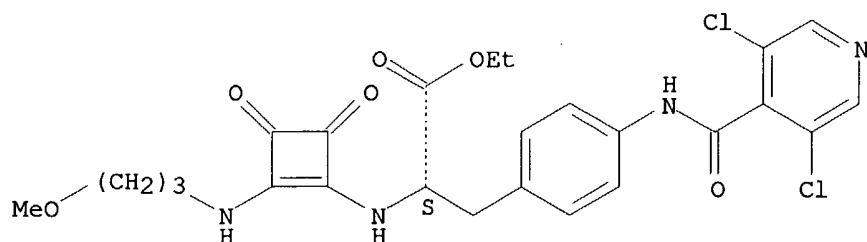
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of squaric acid derivs. as cell adhesion mols.)

RN 312292-13-0 CAPLUS

CN L-Phenylalanine, 4-[[[(3,5-dichloro-4-pyridinyl)carbonyl]amino]-N-[2-[(3-methoxypropyl)amino]-3,4-dioxo-1-cyclobuten-1-yl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

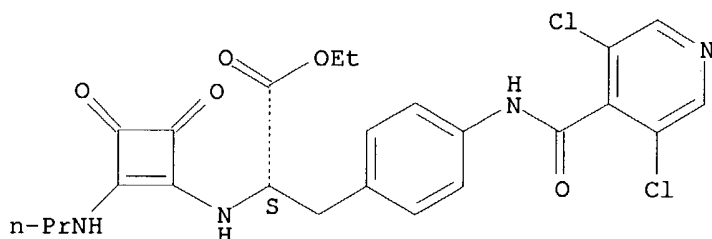


10/081,072

RN 312292-15-2 CAPLUS

CN L-Phenylalanine, 4-[[(3,5-dichloro-4-pyridinyl)carbonyl]amino]-N-[3,4-dioxo-2-(propylamino)-1-cyclobuten-1-yl]-, ethyl ester (9CI) (CA INDEX NAME)

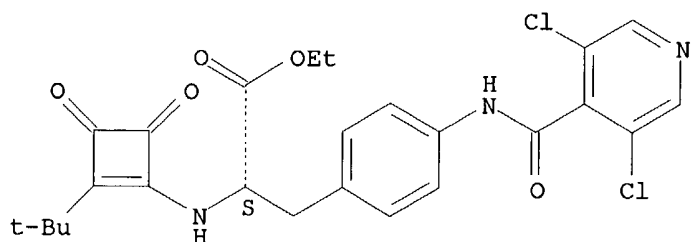
Absolute stereochemistry.



RN 312292-17-4 CAPLUS

CN L-Phenylalanine, 4-[[(3,5-dichloro-4-pyridinyl)carbonyl]amino]-N-[2-(1,1-dimethylethyl)-3,4-dioxo-1-cyclobuten-1-yl]-, ethyl ester (9CI) (CA INDEX NAME)

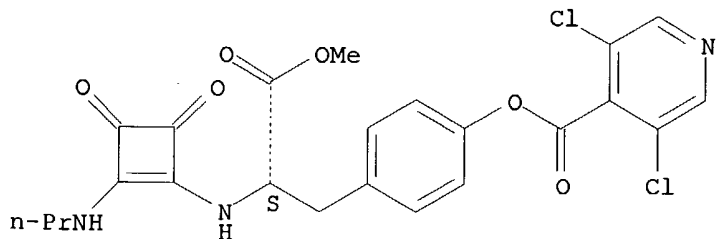
Absolute stereochemistry.



RN 312292-19-6 CAPLUS

CN L-Tyrosine, N-[3,4-dioxo-2-(propylamino)-1-cyclobuten-1-yl]-, methyl ester, 3,5-dichloro-4-pyridinecarboxylate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

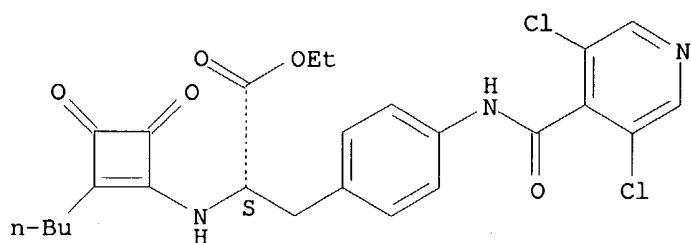


RN 312292-21-0 CAPLUS

CN L-Phenylalanine, N-(2-butyl-3,4-dioxo-1-cyclobuten-1-yl)-4-[[(3,5-dichloro-4-pyridinyl)carbonyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

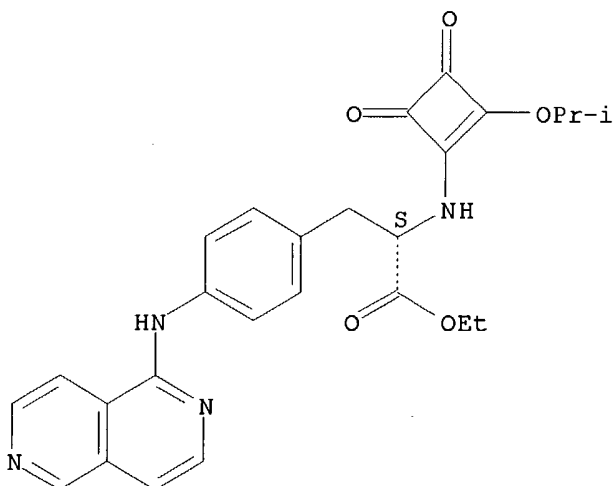
10/081,072



RN 312292-23-2 CAPLUS

CN L-Phenylalanine, N-[2-(1-methylethoxy)-3,4-dioxo-1-cyclobuten-1-yl]-4-(2,6-naphthyridin-1-ylamino)-, ethyl ester (9CI) (CA INDEX NAME)

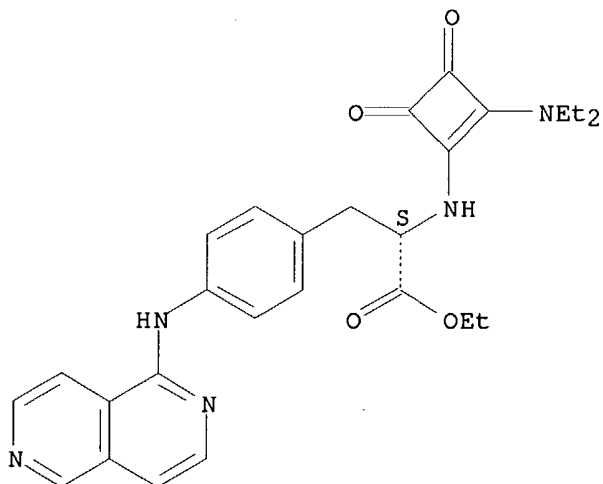
Absolute stereochemistry.



RN 312292-24-3 CAPLUS

CN L-Phenylalanine, N-[2-(diethylamino)-3,4-dioxo-1-cyclobuten-1-yl]-4-(2,6-naphthyridin-1-ylamino)-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



10/081,072

T 2004 ACS on STN

ACCESSION NUMBER:

2000:421084 CAPLUS

DOCUMENT NUMBER:

133:43808

TITLE:

Preparation of 3,4-diamino-3-cyclobutene-1,2-dione derivatives which inhibit leukocyte adhesion mediated by VLA-4

INVENTOR(S):

Lombardo, Louis John; Sabalski, Joan E.

PATENT ASSIGNEE(S):

American Home Products Corporation, USA

SOURCE:

PCT Int. Appl., 59 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

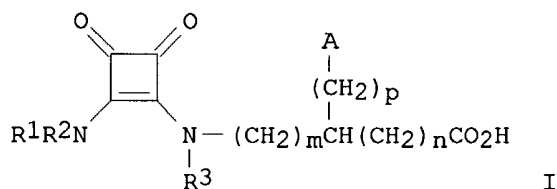
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000035855	A1	20000622	WO 1999-US29369	19991210
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RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
BR 9916211	A	20010911	BR 1999-16211	19991210
EP 1140792	A1	20011010	EP 1999-967265	19991210
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
PRIORITY APPLN. INFO.:			US 1998-211183 A	19981214
			WO 1999-US29369 W	19991210

OTHER SOURCE(S): MARPAT 133:43808

GI



AB Diaminocyclobutenedione amino acid derivs. I (R1 = alkyl, aryl, heteroaryl, aralkyl, heteroaralkyl; R2 = H, alkyl, aryl, heteroaryl, aralkyl, heteroaralkyl or R1R2N form a saturated or unsatd. heterocyclic ring; R3 = H, alkyl, aryl, heteroaryl, aralkyl, heteroaralkyl; A = aryl, heteroaryl; m, n, p = 0-3) were prepared for the treatment of inflammatory and autoimmune diseases. Thus, N-[2-(benzylamino)-3,4-dioxocyclobut-1-enyl]-L-phenylalanine, prepared by treatment of L-phenylalanine Me ester hydrochloride with 3,4-diethoxy-3-cyclobutene-1,2-dione and benzylamine and saponification, showed IC50 for binding of the $\alpha 4\beta 1$ integrin (VLA-4).

IT 274927-11-6P 274927-14-9P 274927-20-7P
274927-22-9P 274927-24-1P 274927-26-3P
274927-29-6P 274927-31-0P 274927-33-2P

10/081,072

274927-38-7P 274927-51-4P 274927-53-6P

274927-56-9P

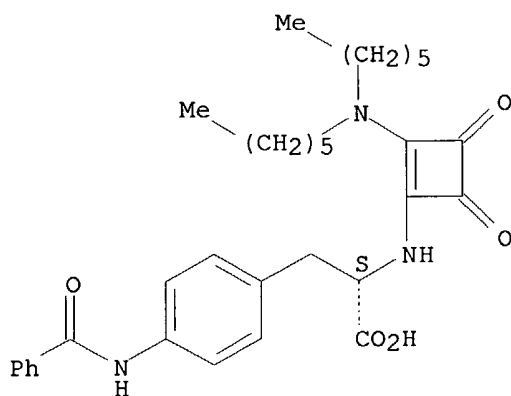
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of diaminocyclobutenedione derivs. which inhibit leukocyte adhesion mediated by VLA-4)

RN 274927-11-6 CAPLUS

CN L-Phenylalanine, 4-(benzoylamino)-N-[2-(dihexylamino)-3,4-dioxo-1-cyclobuten-1-yl]- (9CI) (CA INDEX NAME)

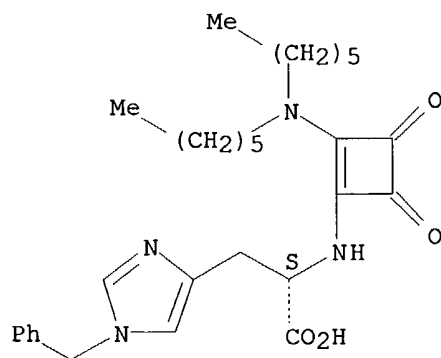
Absolute stereochemistry.



RN 274927-14-9 CAPLUS

CN L-Histidine, N-[2-(dihexylamino)-3,4-dioxo-1-cyclobuten-1-yl]-1-(phenylmethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

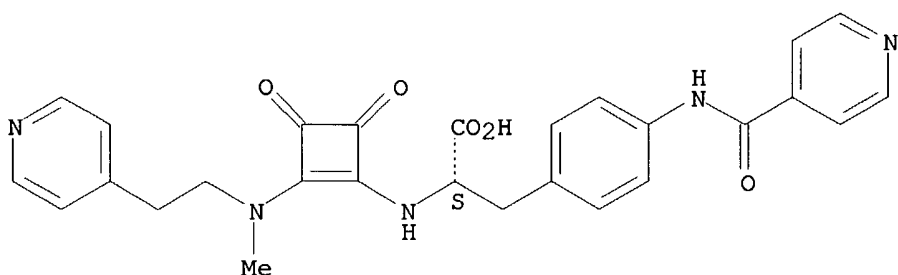


RN 274927-20-7 CAPLUS

CN L-Phenylalanine, N-[2-[methyl[2-(4-pyridinyl)ethyl]amino]-3,4-dioxo-1-cyclobuten-1-yl]-4-[(4-pyridinylcarbonyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

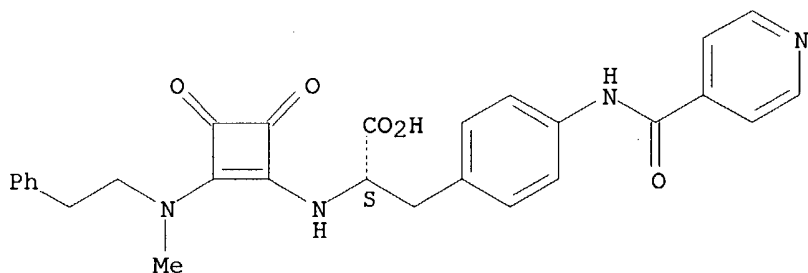
10/081,072



RN 274927-22-9 CAPLUS

CN L-Phenylalanine, N-[2-[methyl(2-phenylethyl)amino]-3,4-dioxo-1-cyclobuten-1-yl]-4-[(4-pyridinylcarbonyl)amino]- (9CI) (CA INDEX NAME)

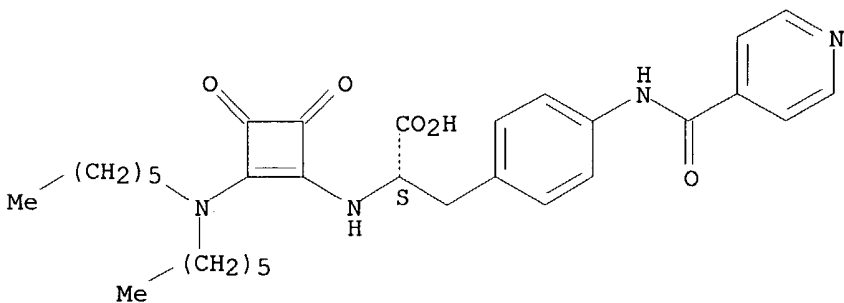
Absolute stereochemistry.



RN 274927-24-1 CAPLUS

CN L-Phenylalanine, N-[2-(dihexylamino)-3,4-dioxo-1-cyclobuten-1-yl]-4-[(4-pyridinylcarbonyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

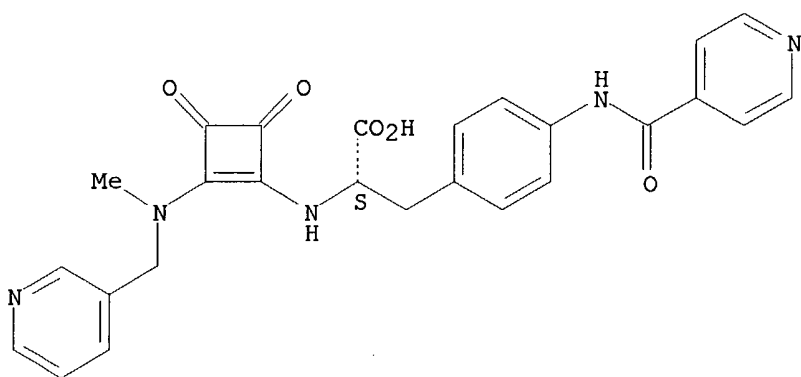


RN 274927-26-3 CAPLUS

CN L-Phenylalanine, N-[2-[methyl(3-pyridinylmethyl)amino]-3,4-dioxo-1-cyclobuten-1-yl]-4-[(4-pyridinylcarbonyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

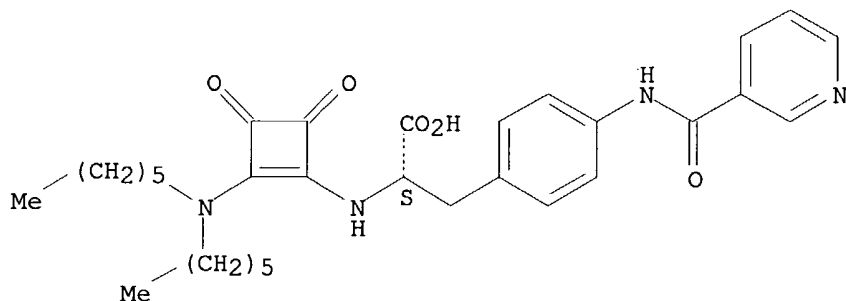
10/081,072



RN 274927-29-6 CAPLUS

CN L-Phenylalanine, N-[2-(dihexylamino)-3,4-dioxo-1-cyclobuten-1-yl]-4-[(3-pyridinylcarbonyl)amino]- (9CI) (CA INDEX NAME)

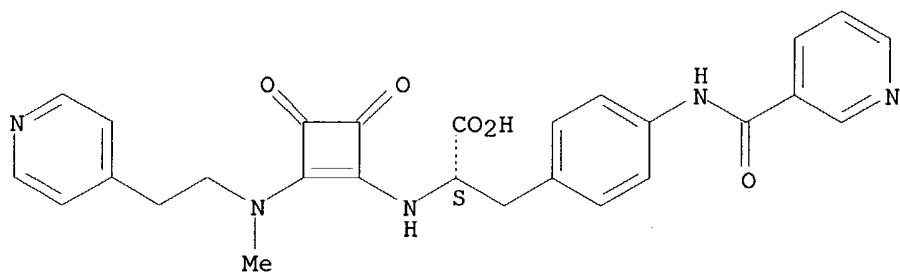
Absolute stereochemistry.



RN 274927-31-0 CAPLUS

CN L-Phenylalanine, N-[2-[methyl[2-(4-pyridinyl)ethyl]amino]-3,4-dioxo-1-cyclobuten-1-yl]-4-[(3-pyridinylcarbonyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 274927-33-2 CAPLUS

CN L-Phenylalanine, N-[2-[methyl(3-pyridinylmethyl)amino]-3,4-dioxo-1-